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# THE TREATMENT OF CORONARY ARTERY DISEASE

A. C. ERNSTENE, M. D.

The five chief manifestations of coronary artery disease are: (1) angina pectoris, (2) coronary thrombosis with infarction of the myocardium, (3) cardiac asthma (paroxysmal cardiac dyspnea), (4) Adams-Stokes syndrome, and (5) congestive myocardial failure. Each of these conditions gives rise to a well-differentiated clinical picture, and the management of each differs in important respects from that of the others. The diagnostic features and treatment of the various syndromes will be discussed in the present communication.

## ANGINA PECTORIS

Angina pectoris is a descriptive term applied to paroxysmal attacks of substernal pain which characteristically are precipitated by exertion or excitement and are relieved promptly by rest. The patient often experiences difficulty in describing the pain and frequently refers to it as a sensation of fullness, pressure, tightness or heaviness in the anterior chest. The distress is of such a nature as to enforce cessation of all activity and at times is accompanied by a sense of impending death. There may or may not be radiation of the discomfort to the neck, jaws or inner aspect of the arms. Glyceryl trinitrate and similar preparations give prompt relief from the symptoms. Death may occur instantaneously during an attack.

The most important measure in the treatment of angina pectoris consists of impressing upon the patient the imperative need for limitation of his activity in order to avoid, so far as possible, the induction of attacks. Hurry and unusual exertion of all kinds must be prohibited. Certain conditions exert an important effect upon the ease with which the pain is precipitated, and the patient must be instructed fully concerning these. The attacks come on with greater readiness during cold weather than during the warmer months. The patient therefore must be advised to reduce his gait during the fall and winter months and must be informed specifically of the greatly added load which walking against a wind or through snow places upon the heart. Residence in a warmer climate should be urged in all cases in which such a change is financially possible. Less exertion usually is required to induce the pain soon after eating than at other times, and occasionally an attack may result from the taking of a large meal without additional activity. Because of this it is important that overeating be avoided and that the patient rest for at least 30 minutes after each meal. Occasionally it is advisable to allow four or five small meals daily rather than three larger ones. The overweight individual should be placed upon a reducing diet, for the loss of excess weight will result in a proportionate diminution in the

demands on the heart during physical activity. Coffee and tea should be allowed only in moderation, and the consumption of tobacco should be reduced to the lowest level the patient will accept. Because straining at stool may initiate an attack in certain persons, suitable measures must be taken to avoid constipation.

Many preparations have been recommended for use in patients with angina pectoris with the aim of increasing blood flow through the diseased coronary arteries, but the clinical effectiveness of most of these drugs remains doubtful. Although the administration of aminophylline and similar preparations in sufficient amounts results in a certain degree of increase in the ability of the patient to do measured work without pain, the magnitude of this increase is seldom such as to be of appreciable help in the regular daily activities of the individual. Most patients appear to do quite as well without drugs of this nature as they do with them, but because an occasional individual is benefited, a short therapeutic trial with one of the preparations is in order in all patients.

The two drugs of thoroughly established value in the management of angina pectoris are glyceryl trinitrate and amyl nitrite. Of the two, the former is to be preferred; it is just as effective as the latter, has a somewhat longer period of action, is less unpleasant to use and less expensive. Only fresh tablets should be employed, and these should be dissolved under the tongue or should be chewed thoroughly before swallowing. For many individuals a 1/200 grain tablet is as effective as a larger amount. The drug is employed not only for the relief of anginal pain but also as a means of preventing the development of attacks. Many patients are forced by the nature of their occupation to perform tasks which regularly precipitate anginal pain, and in these persons the attacks often can be prevented from developing by the use of glyceryl trinitrate shortly before undertaking the unavoidable exertion. In unusual circumstances from 12 to 20 tablets may be used in this manner each day. When attacks are liable to follow a meal, the drug may be given for its prophylactic effect either immediately before or soon after eating. The frequent use of nitroglycerine in this manner does no harm and often enables the patient to get along comfortably for a long time. It does not excuse him, however, from avoiding unnecessary types of activity that may bring on an attack.

In persons who are inclined to worry or in whom anginal pain is induced by emotional upsets, sedatives are indicated and may have a very beneficial effect. Occasionally an appreciable increase in exercise tolerance follows the use of whiskey or brandy in doses of one-half ounce or one ounce with each meal. Digitalis is employed only in the presence of such evidence of myocardial insufficiency as dyspnea on limited activity, passive congestion of the lungs, and edema of the lower extremities.

Of the various surgical measures that have been employed in the treatment of angina pectoris, alcohol injection of the upper four thoracic sympathetic ganglia on one or both sides appears to be the safest procedure and to be equal to any other in effectiveness. This method of treatment does not change the condition of the coronary vessels but it does afford the patient partial or complete relief from his attacks and may therefore enable him to remain self-supporting for a considerable length of time. Neuritis of the infiltrated intercostal nerves is a rather common complication following injections but is seldom a source of great complaint in those who have had severe anginal attacks. This method of treatment is worthy of wider application than at present but its use should be restricted to those cases in which the attacks can be controlled in no other way.

The work of Beck and his associates[1] in establishing a new blood supply to the heart by grafting a part of the pectoral muscle upon the myocardium constitutes a direct attack on the underlying coronary artery disease. The clinical results have been distinctly encouraging and the further progress of the work will be watched with great interest.

### Coronary Thrombosis

The clinical picture of acute coronary thrombosis is too well known to warrant detailed description at this time. The pain is similar to that in angina pectoris but is more severe and of longer duration. Symptoms of shock of mild or severe degree usually appear soon after the onset, and fever and leukocytosis generally develop within the first 24 hours. The erythrocyte sedimentation rate becomes elevated. A pericardial friction rub may appear at any time during the first few days after the attack and may last for only a few hours or for several days. The electrocardiogram will show characteristic changes in practically all cases of coronary thrombosis if records are made at daily intervals and if both standard and precordial leads are used.

The first aim in the treatment of acute coronary thrombosis is to relieve the pain. For this purpose morphine sulfate should be administered by hypodermic injection as promptly as possible. The initial dose is usually one-fourth grain but whenever the pain is exceptionally severe one should not hesitate to administer one-half grain. Subsequent doses of one-fourth grain should be given at intervals of one-half hour or so if the distress continues unabated. At times, it may be necessary to administer as much as one grain within the first hour or two. The patient should be placed in bed as soon as possible after the onset of symptoms and should not be disturbed by frequent examinations. Because of the shock and profuse perspiration which often are present, the body should be kept warm and, as soon as the patient is more comfortable and is free from nausea and vomiting, fluids should be offered in frequent small amounts. Stimulants, such as caffein sodium benzoate, are

administered only if the systolic blood pressure falls below 80 mm. of mercury.

In the more severe attacks of coronary thrombosis which are accompanied by cyanosis and intense dyspnea, the administration of oxygen should be instituted as promptly as possible, preferably by means of an oxygen tent. Not only does this measure reduce the cyanosis and dyspnea but it may also lessen the intensity and shorten the duration of the pain.

After the pain and initial shock have been controlled, the majority of patients require little medication. It appears advisable, however, to administer quinidine sulfate in doses of 0.2 gm. (3 grains) two or three times a day as a possible prophylactic against the development of ventricular paroxysmal tachycardia and ventricular fibrillation. Aminophylline in doses of 0.1 gm. (1½ grains) may be given three or four times a day but its value is hard to estimate. Sedatives in small divided doses may be necessary during the day or at bedtime to control restlessness. Digitalis is employed only in the event of congestive myocardial failure or when there is auricular fibrillation with a rapid ventricular rate. The diet should be simple and should be limited to a value of 800 or 1000 calories. If the bowels do not move spontaneously, enemas should not be administered until after the second or third day.

The emphasis in treatment should be placed on the necessity for absolute rest. The patient should be fed and should not be allowed to help in changing his position for at least two weeks, and the total period of rest in bed should be from six to eight weeks. The erythrocyte sedimentation rate is a helpful guide in this respect; rest is enforced until the rate has become stationary at a normal or nearly normal level. After the period in bed, the patient is permitted to be up for short and gradually increasing lengths of time daily but is not allowed to return to his business activities for 3 to 12 months, depending upon the severity of the attack.

The most important complications of coronary thrombosis are: (1) sudden death due to rupture of the ventricle or to ventricular fibrillation, (2) ventricular paroxysmal tachycardia, (3) congestive heart failure, and (4) embolic accidents. Sudden death and ventricular paroxysmal tachycardia occur most commonly during the first two weeks after the occlusion. Ventricular tachycardia may be a forerunner of ventricular fibrillation or it may be directly responsible for the development of congestive heart failure. Its onset calls for the administration of increased amounts of quinidine sulfate. Congestive myocardial failure is treated by the usual measures, including the use of digitalis. After acute coronary thrombosis, a mural thrombus commonly forms on the endocardial surface of the infarcted myocardium. Embolic accidents, the result of dislodgment of portions of the thrombus, may occur at any time during

the first six weeks after the attack but are most common during the earlier part of this period. The emboli may lodge in any part of the pulmonary or systemic circulation and their treatment usually is limited to symptomatic measures.

### Cardiac Asthma

Coronary artery disease is a common cause of that form of paroxysmal dyspnea to which the term cardiac asthma is applied. The attacks of dyspnea are due to failure of a damaged left ventricle and usually occur at night although occasionally they are induced by exertion. Because of relative weakness of the left ventricle, an increased amount of blood accumulates gradually in the pulmonary vessels during sleep in the recumbent position. The vital capacity, which is already diminished, is still further reduced as the degree of pulmonary congestion increases, and all that is now necessary to initiate the attack of cardiac asthma is some factor which acts as the trigger mechanism. Cough, Cheyne-Stokes respiration, noise, disturbing dreams and the urinary reflex most commonly supply this factor. The patient wakens with respiratory distress and is forced to sit up or stand in order to breathe. Asthmatic breathing develops, with both inspiratory and expiratory difficulty, and as the attack progresses acute pulmonary edema may supervene.

The two most important measures in the treatment of attacks of cardiac asthma are morphine and the upright position. Morphine exerts its beneficial effect by depressing the respiratory and vasomotor centers in the medulla and by reducing the patient's apprehension and anxiety. The drug should be administered hypodermically as early in the attack as possible, usually in doses of one-fourth grain, and should be repeated if the patient does not appear to be improved within fifteen or twenty minutes. The relief which the patient experiences in the upright position probably is due principally to the increase in the vital capacity which accompanies the change from the recumbent to the erect posture. There is evidence also that the minute volume output of the heart is decreased in the upright position, and, of course, any reduction in cardiac work would lead to an improved state of the pulmonary circulation.

Morphine and the upright position at times may fail to relieve the patient sufficiently and other measures must be employed. Aminophylline may be given by intravenous injection in doses of 0.48 gm. diluted with physiologic solution of sodium chloride or 50 per cent dextrose solution and may result in prompt improvement. The beneficial effect of the preparation is attributed principally to its action on the coronary circulation[2] but the drug also causes a diminution in the degree of bronchial spasm[3]. In the absence of anemia, venesection should be carried out with the removal of 250 cc. to 500 cc. of blood. This may result in prompt and lasting relief, particularly in patients who present engorge-

ment of the peripheral veins. Venesection reduces the circulating blood volume, and as a result, the work of the heart is diminished and pulmonary congestion is lessened. An effect similar to that of venesection may be obtained by applying blood pressure cuffs to the four extremities and inflating them to a pressure just above diastolic blood pressure. The administration of oxygen by means of a tent or by nasal catheter is also a measure of great value and should be instituted as promptly as possible.

In patients in whom cardiac asthma progresses to acute pulmonary edema in spite of the above measures, either strophanthin or digitalis should be given intravenously. It is, of course, essential to ascertain that these patients have not received digitalis earlier.

A patient who has experienced an attack of cardiac asthma due to failure of the left ventricle should be treated as any other individual who presents evidence of impaired myocardial reserve. Complete digitalization and the subsequent administration of daily maintenance amounts of the drug are indicated, and in subjects who have had but mild attacks, this measure alone may suffice to prevent the recurrence of paroxysms. In those who have suffered more severe attacks, a period of absolute rest is advisable and should be followed by strict limitation of activity. Restriction of fluids and the administration of diuretic drugs also are valuable measures. At times, the intravenous injection of hypertonic glucose solution (50 to 100 cc. of a 25 or 50 per cent solution daily for several days) may be helpful in diminishing the frequency of attacks. Because cardiac asthma due to left ventricular failure usually occurs at night and the onset of the seizure is favored by the recumbent position, the patient should be instructed to sleep well propped up in bed. Sedatives also should be given to insure sound sleep since the attacks generally are precipitated by some factor which tends to waken the patient.

## Heart Block

Coronary artery disease is the most common cause of auriculoventricular block. Simple prolongation of auriculoventricular conduction time is observed at times in individuals who have no symptoms referable to the cardiovascular system. More commonly, however, just as in the higher grades of heart block, the patient presents evidence of reduced myocardial reserve, and in such cases the cautious administration of digitalis is indicated. The treatment should be carried out with electrocardiographic control, and if the degree of block increases, the drug should be discontinued. In favorable cases, suitable amounts of digitalis not only relieve the symptoms of myocardial insufficiency but may also reduce the degree of block or abolish it entirely.

The higher grades of heart block, and particularly complete auric-

uloventricular dissociation, may be complicated by Adams-Stokes attacks due to temporary standstill of the ventricles. The seizures are characterized by dizziness, syncope or convulsions, depending upon the duration of the ventricular asystole. Adams-Stokes attacks are not common, but individuals in whom they occur are liable to have repeated seizures. The actual attacks seldom call for treatment, and therapy is directed toward preventing their recurrence. Occasionally, however, the standstill may be of such duration as to necessitate the intracardiac injection of epinephrine and this procedure may be directly responsible for the saving of life. The most effective drugs for preventing recurrent attacks are epinephrine (0.5 cc. to 1.0 cc. of the 1:1000 solution) by intramuscular injection every 3 or 4 hours and ephedrine sulfate (gr. $\frac{3}{8}$ or gr. $\frac{1}{2}$) by mouth 3 or 4 times in 24 hours.

## Congestive Heart Failure

Coronary artery disease often results in the gradual development of symptoms and signs of congestive heart failure instead of the more dramatic episodes of angina pectoris, coronary thrombosis, cardiac asthma or Adams-Stokes seizures. Treatment does not differ from that of myocardial failure due to other types of heart disease and consists principally of absolute rest in bed, the proper administration of digitalis, sedatives, and diuretic drugs, restriction of the fluid intake, and, less often, venesection and the mechanical removal of fluid from the thorax or abdomen.

## Summary

The most common manifestations of coronary artery disease are angina pectoris, coronary thrombosis, cardiac asthma, the Adams-Stokes syndrome, and congestive heart failure. The treatment of each of these conditions has been summarized.

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# DECAPSULATION OF THE KIDNEY IN THE COURSE OF CELIAC GANGLIONECTOMY FOR ESSENTIAL HYPERTENSION

GEORGE CRILE, M. D.

Many years ago Edebohls of New York proposed the operation of decapsulation of the kidneys for chronic nephritis and hypertension. I performed this operation at that time in a number of cases. In many parts of the country there were reports of some very good results; other results were entirely negative. That was true in my own series. The operation, however, did not yield sufficiently good results to justify its continuance although it did modify favorably many of the cases. The indication for the operation, then, was in the late stage of the disease.

At the present time the success of various procedures on the sympathetic system in the treatment of essential hypertension is such that patients are beginning to seek treatment in the earlier phase of the disease, although the largest numbers unfortunately still consult us in the late or terminal phase.

In any incision we make for celiac ganglionectomy, the kidney and its blood supply is completely exposed; indeed, we are obliged to draw the kidney away from the field of operation to show the ganglion more clearly. Therefore, it requires but a few minutes to decapsulate the kidney, and this operation we have now performed in six cases. It is too early to evaluate this method, but the first indications seem to be that it has contributed something in addition to celiac ganglionectomy.

One reason we have no hesitation in adding this trifling procedure to celiac ganglionectomy itself is because the operative risk is now negligible, as in the last 119 operations there have been no surgical deaths. We can, therefore, with confidence, add this slight, additional maneuver.

It was apparent in these six instances that the more severe cases of hypertension showed a very decided congestion of the raw surface of the kidney itself when the capsule was removed, and there was slight oozing for quite a little while. This may signify renal congestion which could well have exerted some interference with renal function.

# HEADACHE CAUSED BY ARTHRITIS OF THE CERVICAL SPINE

C. L. HARTSOCK, M. D.

Arthritis and its allied conditions, (myositis, fibrositis, fascitis and tenosynovitis, involving the bones and attachments of the cervical spine and base of the skull) produce a type of cephalalgia that often causes considerable diagnostic and therapeutic difficulties. This form of headache occurs almost as frequently as ocular and migraine headaches but it has not been appreciated to the same extent because it is attributed so often to other etiological factors. Diagnosis must be made largely from the history. Fortunately, this is quite characteristic in most cases and is as typically diagnostic as the true migraine syndrome.

The headache invariably begins in the occiput but has a tendency to spread upwards and forward into the temporal regions as it becomes more severe. If the patient is able to critically analyze the onset, the pain will really be placed in the cervical muscles with a feeling of stiffness and soreness, especially of the attachment of the trapezius muscle to the skull. Of extreme diagnostic importance is the tenderness of this tendon attachment. The headaches occur periodically at first, lasting three to four days, a trifle longer than the usual migraine headache. There is a tendency to have long sieges of constant headache which may become a permanent daily headache. In a great majority of patients the headache comes on early in the morning and usually wakens them from sleep.

Most patients notice the relation of the headache to exposure to drafts, such as riding in the back seat of a car, sitting in an air-cooled movie theater, and following wetting of the hair, especially if there is also a draft on the head while wet. Drying the hair with dryers often brings on the headache. Another common cause is anything that will cause tenseness of the muscles of the neck for a long period of time, such as driving a car for long distances, sewing, stenographic work, etc. If there is an associated eye muscle error, focusing the eyes for long periods of time is doubly liable to cause the muscles of the neck to be more tense.

The indirect cause, such as drafts, wet hair, and eye strain, sometimes occurs the previous day and is frequently overlooked unless attention is directed to this and then the relationship usually can be recalled. Sometimes, even the removal of a small amount of protection from cold, such as when a man has his hair cut, is enough to cause this myalgic type of headache. Crepitus frequently accompanies the headache and is audible when the head is turned from side to side. Flexing the head forward and stretching the neck muscles increase the pain. Frequently the patient exhibits a characteristic motion of bending the

head backwards and, with the palm of the hand, stroking the back of the head with a downward movement towards the neck. This usually gives some relief. Many patients have learned that heat and massage will give great relief. As a rule, there is no associated nausea and vomiting.

The headache occurs mostly in middle aged people who are approaching the osteo-arthritic age group but occasionally some patients in the early twenties are seen. In such patients, there is more possibility of an infectious process being present whereas in most patients the arthritic process seems to be of the metabolic type related to osteo-arthritis. If the patient is over 50 years of age, there usually is fairly marked roentgen evidence of this type of arthritis in the cervical spine. A history of arthritic pains in either location, especially the lower back, knees, and shoulders, is further confirmation of the nature of the occipital headache.

There will be minor variations in different cases but there always will be enough salient features on the basis of history alone to separate this type of headache from the great group of cephalalgias.

When the headache persists for long periods of time or if it eventually becomes constant, it can be a major cause of disability. In persistent cases, intracranial lesions are frequently suspected and this incurs great expense and suffering in efforts to seek the etiology.

Due to the frequent association of hypertension and osteo-arthritis in the same patient, the headache is frequently attributed to hypertension. I do not mean to imply that there is a causal relationship between hypertension and osteo-arthritis. They both are degenerative diseases of age and both occur more commonly in the older age group, especially in more obese individuals.

If this type of headache can be so easily recognized from the history alone, and possibly a simple examination of the cervical region, what other examinations are indicated to help in the solution? The investigation should first be directed along the usual lines for arthritis. Obvious foci of infections should be removed but the fallacy of considering osteo-arthritis as an infectious disease and attempting to treat it as such cannot be emphasized too strongly. Chemical and metabolic studies are more important. An increased glucose tolerance, suggestive of a mild diabetes, sometimes is present and is most helpful in the dietary management.

A low basal metabolic rate is the rule and again a clear indication for therapy that is most beneficial. In selected cases, the blood uric acid should be studied. Studies of the gastrointestinal tract, especially for colonic and biliary stasis, are often helpful in outlining a successful therapeutic regimen. Achlorhydria may afford an excellent clue.

Examination of the eyes should never be omitted in any headache and should be done in this type although in reality it is not a true headache. Refractive errors may be a factor but of great importance is a careful measurement of the muscle balance. The muscles are definitely unbalanced in a very high percentage of cases.

It might be said then that this headache is therefore strictly an ocular headache but there is too much evidence that the eyes act only as an aggravating factor in focusing strain on the cervical muscles and determining the site of election for the arthritic process.

Since the treatment of periodic headaches has been so notably aided by allergic management, the question often comes up concerning the advisability of studying these patients from an allergic viewpoint. We have been disappointed in the results of allergy studies in this type of headache and no longer advise such studies unless the patient is a proved allergic individual in other respects.

One of our patients formerly had definite migraine with nausea, vomiting, and unilateral frontal headaches. This type of headache ceased and the typical arthritic headache developed. Foods that formerly brought on the sick, bilious headache would also precipitate the occipital headache but avoiding these foods would not prevent other causes from bringing on the occipital headaches. Caution, of course, usually dictates that these patients should have a spinal puncture to rule out the many causes for headache over the diseases of the central nervous system. Eventually, however, one gains almost enough confidence in clinical judgment to forego this expensive and at times incapacitating study (postspinal puncture headache).

Roentgen examination of the cervical spine may, as mentioned before, reveal an osteo-arthritic process but its absence does not affect the diagnosis when all the other evidence is positive. Treatment should be both preventive and palliative. All causes of excessive fatigue should be eliminated as far as possible. Care should be taken to avoid drafts. This may be done by wearing a wool covering over the back of the neck when exposed to drafts, especially during sleep. Eye strain should be avoided and muscle errors corrected as far as possible by exercises, glasses and muscle operations. When the patient knows of definite causative factors, a small amount of acetyl salicylic acid at bedtime will often prevent the headache. If the headache develops, heat and salicylates administered early will often give quick relief; if delayed, they frequently are futile. Heat and massage, especially the more constant type, are of utmost value. General arthritic measures, such as a low carbohydrate diet with increased vitamins, especially vitamin B, a reduction in weight if obese, anticonstipation measures, and mild salines in certain cases, are all helpful and useful measures. We have

observed some help from cholegogues. Dessicated thyroid should be given in tolerance doses. Cincophen even should be used in some of the more obstinate cases. Care should be taken in the administration of this drug however. The improved forms of physiotherapy offer the most help to these patients. Orthopedic measures such as continued head traction are occasionally necessary.

The prognosis is entirely in relation to the frequency and severity of the headaches and the ability of the patient to undergo treatment—just as in any case of arthritis.

In conclusion, there is a very common, very typical type of headache due to arthritis of the cervical spine which is frequently misdiagnosed as being due to other causes and therefore is not adequately treated from its true etiological nature.

# WILMS' TUMOR (ADENOMYOSARCOMA) OF THE KIDNEY IN CHILDREN

*Report of a Case*

C. C. Higgins, M. D. and F. L. Shively, Jr., M. D.

Wilms' tumor of the kidney is a topic of considerable discussion today by both the medical profession and the laity. The tumor was recognized as early as 1872 and has been a subject of conjecture since its first description. In this year, Eberth[1] presented an accurate description of the neoplasm. Prior to this time any tumor of the kidney, regardless of the age of the patient, was classified as being carcinomatous in nature.

Wilms' tumor of the kidney is a mixed cell tumor and may contain any or all of the derivatives of the three germinal layers. Because of the multiplicity of tissues, many theories have been advanced as to its derivation. In 1872, Eberth[1] suggested the theory that the tumor was derived from remnants of the wolffian body. Cohnheim[2], in 1875, attributed the origin to aberrant germ plasm from the primitive segments and Ribbert[3], in 1886, in agreement with Cohnheim, stated the tumor was derived from a totipotent blastomere. In 1894, Birch-Hirschfeld[4] concurred with Eberth upon its origin from the wolffian body. Brock[5], in 1895, averred that the derivation was from embryonic cell inclusions embedded in the urogenital fold.

One can readily observe that there was much confusion as to the exact origin or derivation of this neoplasm. This led Wilms[6], to write his important monograph on the origin and derivation of this tumor. His theory at present is the one most widely accepted. He stated that the wolffian body could not be expected to produce all of the tissues so commonly found. He assumed that they were derived from primitive undifferentiated mesodermal tissue of the type that in the course of normal development gives rise to the myotome (skeletal muscle), sclerotome (vertebrae), nephrotome (wolffian body anlage), and mesenchymal tissue which gives rise to smooth muscle.

Several theories have been advanced in recent years, but most of these have been, more or less, reiterations of the theories mentioned previously. Ewing[7], however, in 1934, favored the conception that these tumors are derived from the renal blastoma. This view attributes a prominent part to metaplasia, thus accounting for the adult types of tissues found, namely, squamous epithelium, striated muscle, cartilage, and bone.

## Report of Case

The patient was a girl, 4 years of age, who was admitted to the Clinic on May 4, 1939. The mother had observed a protuberant abdomen and stated that one side of the child's body was larger than the other.

The following history was obtained from the mother. The child was delivered normally, and was physically perfect in all respects. The patient had been given cod liver oil and orange juice since birth. The first difficulty was encountered when it became necessary to feed the child from the bottle, at which time marked constipation began and an umbilical hernia developed. She was subsequently placed on skim milk and the progress was quite satisfactory. At the age of about one year severe otitis media developed, the temperature being elevated for five weeks. This condition finally subsided and the child was in good health for the following year. It was then deemed advisable to place the patient on a high fat diet because of malnutrition. Following the use of this diet, severe vomiting, marked diarrhea, and a high fever developed. Urinalysis at this time revealed the presence of sugar, acetone, albumin, and pus. These urinary findings had recurred upon two other occasions when the so-called fat diets were administered and always subsided in about one week. Thyroid extract was advised by the attending physician but this was not given over an extended period of time because of an elevation of temperature which followed its administration.

Since the age of two years the patient had had a potbelly, accompanied by a considerable amount of gas which required an enema every night in order that she could sleep. The bowels, however, had been regular for the past six months, the stool being normal in all respects. The mother had also noticed that the left side of the body was larger than the right but was indefinite as to the duration of this symptom.

A few days prior to admission, the temperature became elevated, accompanied by an occasional pain in the abdomen. The patient also complained of frequency, nocturia, burning, and dysuria; pyuria was noted. Blood had not been observed in the urine. There were no respiratory or cardiovascular complaints.

*Physical Examination:* The patient was a well developed, well nourished girl whose height was 42 inches and weight 40 pounds. The temperature was 101.8° F., pulse rate 120 per minute, respirations 24, and blood pressure 100/70. The skin was pale and of good texture. Examination of the eyes, ears, nose, and mouth was negative. The thyroid was not enlarged. The chest, lungs, and mediastinum were normal and there were no abnormal findings in the heart. Examination of the abdomen revealed it to be large, prominent, and somewhat distended. There was an indefinite, tender, very large, irregular mass filling the entire left side of the abdomen. The right side was distended with gas. A small umbilical hernia was present. Examination of the external genitalia and rectum was negative. The right arm and leg were definitely smaller than the extremities of the opposite side but, however, there was no loss of power on the affected side. The cranial nerves and the reflexes were normal.

*Laboratory Findings:* Examination of the blood showed 3,950,000 red cells with 71 per cent hemoglobin, and 8,300 white cells with a differential count of 51 per cent neutrophils, 1 per cent eosinophils, 43 per cent lymphocytes, and 4 per cent monocytes. The level of blood sugar was 79 mg. per 100 cc. Wassermann and Kahn tests of the blood gave negative reactions. Urinalysis

showed the pH to be 6.0, a trace of albumin, but no sugar was present; an occasional white blood cell and a rare red blood cell were found.

The initial roentgenogram of the abdomen revealed the lumbosacral region to be normal. No suspicious shadows were seen in the urinary tract. The kidneys could not be visualized because the intestines were distended with gas.

An intravenous urogram showed the kidneys to have prompt and good function. The right kidney was high but apparently normal. The left kidney was very large, extending low into the left abdomen. A definite filling defect was present (Fig. 1).

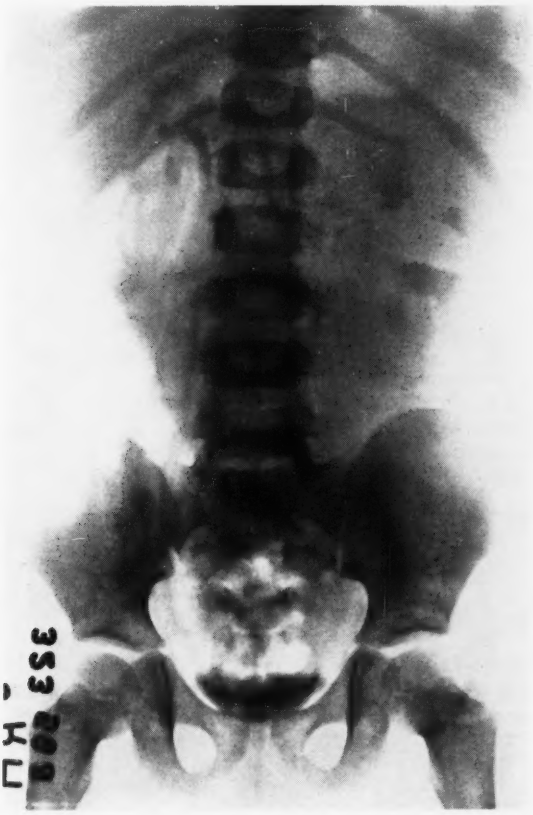

FIGURE 1: Intravenous urogram showing large filling defect in left kidney.

Roentgen examination of the chest was essentially normal. There was no evidence of metastasis.

A diagnosis of Wilms' tumor of the kidney was made and, after considering the above information, it was deemed advisable to administer a course of deep roentgen therapy. This was carried out in the following manner by Dr. R. D.

Bacon of Erie, Pennsylvania. Roentgen rays were applied in three ports, the anterior, lateral, and posterior renal areas, 200 kilovolts at 50 cm. with a Thoraeus filter and a half-value layer of 1.45 mm. of copper being used. The wave length was estimated as being .140 angstrom unit. In the treatment a portal 15x10 cm. vertical and transverse diameters respectively was used. Treatments of 100 r units daily were given until 1,700 r units had been administered to each of the three ports, making a total of 5,100 r units. It was estimated that this irradiation represented approximately 2,500 r units to the kidney pedicle.

The patient tolerated the above therapy very well, but developed a moderate radiation dermatitis with desquamation of the surface epithelium. This healed promptly in a few weeks.

An excellent result was obtained in that the patient lost but little weight while the abdominal circumference was reduced from 25 inches to 21 inches, and the circumference at the rib margin was reduced from 25 inches to 19.5 inches. Nephrectomy was advised, but it was thought best to postpone the surgical procedure for an additional three weeks, so that the patient could secure all possible benefit from the irradiation.

The patient was admitted to the Cleveland Clinic Hospital on June 29, 1939. The laboratory findings were as follows: Examination of the blood revealed 4,150,000 red cells with a slight anisocytosis, 65 per cent hemoglobin, and a color index of 0.78. There were 3,500 white cells, the differential count showing 60 per cent neutrophils, 3 per cent basophils, 24 per cent lymphocytes, and 12 per cent monocytes. No abnormal white blood cells were found. The blood platelets were normal. The level of the blood urea was 45 mg. per 100 cc. Blood Wassermann and Kahn tests gave negative reactions. Urinalysis showed the pH to be 6.0, and specific gravity 1.016, a trace of albumin was noted and no sugar was present; many red blood cells and a moderate amount of amorphous crystals were found. A vaginal smear for the gonococcus was negative.

On the following day operation was performed under avertin anesthesia. It was necessary to administer a small amount of ether during the course of the procedure. A left nephrectomy was done in the routine manner; no unforeseen circumstances were encountered during the operation. The course in the hospital was uneventful and the patient was discharged on the twelfth postoperative day.

*Pathological Description of Kidney Tumor:* The gross specimen consisted of a left kidney which weighed 182 grams and measured 12x5x5 cm. (Fig. 2). A small amount of fatty tissue was attached to the capsule. The ureter was divided approximately 1.5 cm. from the ureteropelvic junction. The upper pole, calices, and pelvis appeared to be normal. At the lower pole of the kidney there was an encapsulated tumor mass which measured 4.5x4.5x4.5 cm. It was sharply marked off from adjacent kidney tissue but was covered by the kidney capsule. The tumor had a mottled, hemorrhagic surface, with a large, irregular, central hyalinized scar around it, in which there were numerous small cystic areas varying from 0.5 to 1.5 cm. in diameter. The tumor tissue was spongy, edematous, hemorrhagic, and the cut surface had a mucoid appearance.

Immediately above the foregoing nodule and situated beneath the capsule on the lateral border was a second encapsulated, cystic, tumor mass 1.5 cm.

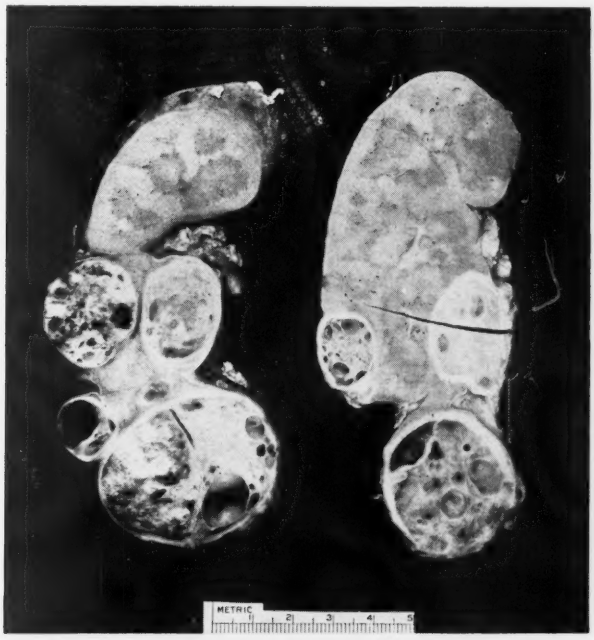


FIGURE 2: Gross specimen. Wilms' tumor at inferior pole. Note normal renal parenchyma at superior pole.

in diameter. This tumor was large and cystic, with little remaining solid neoplastic tissue. Deeply situated in the kidney just above the first tumor nodule described was a third small, encapsulated tumor nodule about 1 cm. in diameter which was solid and hemorrhagic but not cystic. On the mesial surface of the kidney at the lower pole of the hilum, was a fourth encapsulated tumor nodule measuring 2.5x2.0 cm. on the cut surface. Opposite the fourth tumor and embedded in the lateral border of the kidney, was a fifth encapsulated tumor measuring 2.8x2.4 cm. on the cut surface. This consisted of solid, fairly cellular, friable, yellowish-white tumor tissue with a few quite small cystic and hemorrhagic areas, but with very little hyalinization. On the mesial surface near the lower pole of the hilum there was a sixth small encapsulated tumor nodule 1 cm. in diameter, which had a solid white uniform cut surface. The tumor was solid, firm, elastic, and without cysts, areas of necrosis or hyalinized scars. At the same level near the lower pole on the lateral border was an eighth encapsulated tumor measuring 1.8x1.3 cm. on the cut surface. The tumor had numerous small cystic spaces. On the anterior surface and occupying the middle third of the kidney was a ninth tumor module less well encapsulated, having a very dense hyalinized peripheral zone and an irregular central zone composed of uniform, quite cellular, yellowish-brown tumor tissue, grossly suggestive of hypernephroma.

There was no grossly identifiable invasion of the pelvic veins. The tumor nodules did not involve the pelvic mucosa.

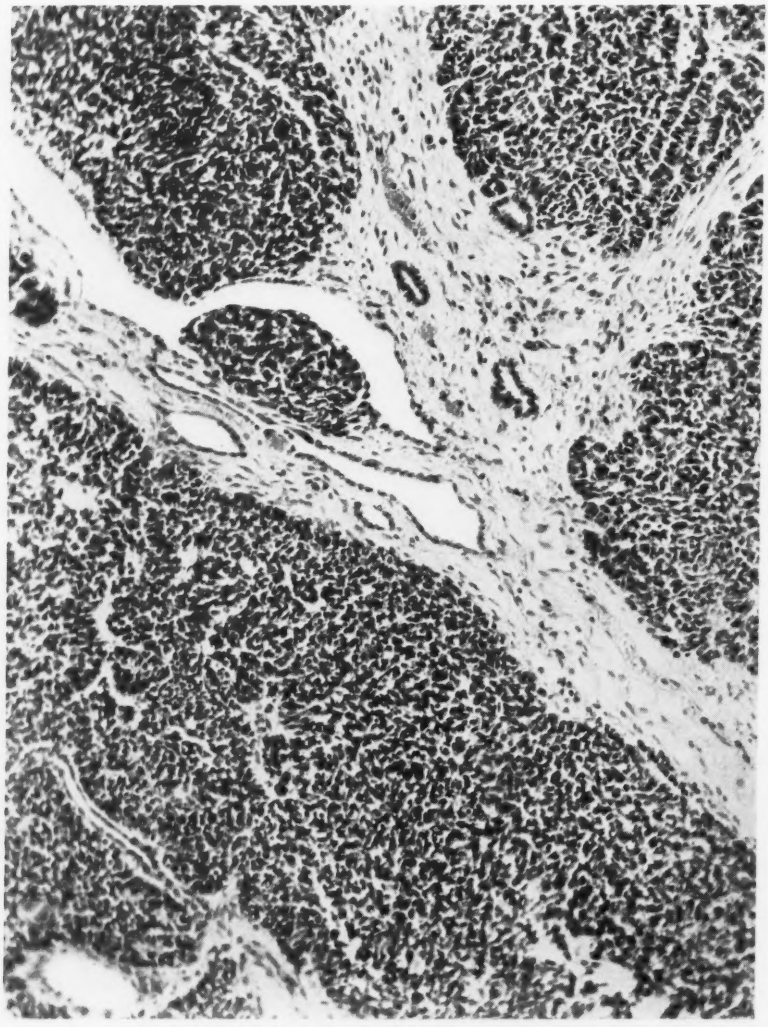

FIGURE 3: Microphotograph taken from a typical area in tumor showing similarity of cell growth and rather well marked hyalinization, necrosis, and cicatrization.

*Microscopic Examination:* Numerous sections from the various areas described above showed an essentially similar type of growth in all nodules (Fig. 3). There were differences due probably to variations in the degree of differentiation, degenerative changes, and also possibly to the effect of irradiation. All of the nodules appeared to be quite well localized or encapsulated and consisted of highly undifferentiated or embryonal cells of the epithelial type, showing varying degrees of differentiation toward what appear to be immature renal tubules and in some instances glomeruli. There was

a great deal of loosely arranged, edematous stroma with areas of hyalinized degeneration, necrosis and cicatrization. There were areas of recent and old hemorrhage, of inflammatory reaction, phagocytosis of blood pigment and large phagocytic cells containing lipoid material. In none of the sections was there any cartilage. In one section there were several small plaques of well differentiated bone, probably of metaplastic origin (Fig. 4). No neoplastic muscle tissue was found in any of the sections.

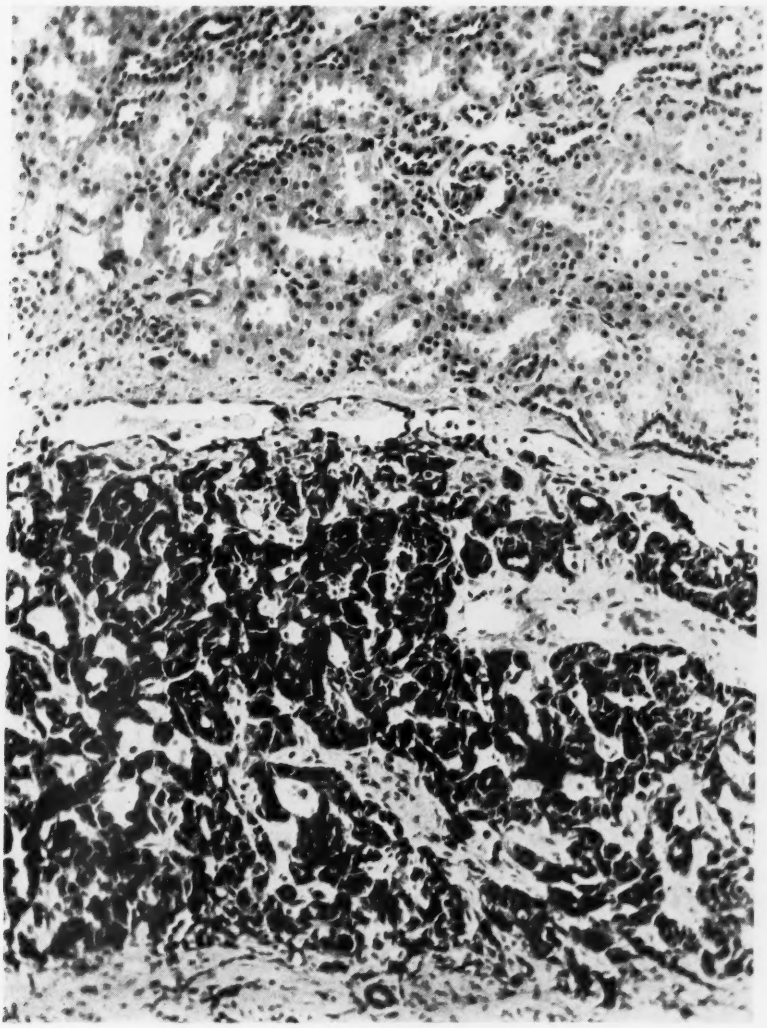

FIGURE 4: Microphotograph of section taken from an area showing immature renal tubules and scattered areas of differentiated bone.

*Follow-Up:* In view of the fact that the patient obtained such a good result from the preoperative irradiation, it was deemed advisable to continue the roentgen therapy postoperatively. This was done under the direction of Dr. Bacon. From July 11 to August 14, 1939, the patient had received eleven treatments of 100 r units successively to each of the three renal ports. This therapy is to be continued for the ensuing 6 weeks until a dose of 1,200 r units has been given to each port, making a total of 3,600 r units.

Together with the radiation therapy the attending roentgenologist administered 600 units of thiamine chloride (vitamin $B_1$) daily in an attempt to obviate any undue gastrointestinal symptoms.

According to the last report, 2 months after the operation, the child is gaining weight and her general condition is excellent.

## Discussion

The symptoms as a rule are not referable to the urinary tract but are general in nature. The most frequent symptom is that of an abdominal tumor. This is usually noticed by the mother, who states that the child's abdomen has grown progressively larger over a period of time and the enlargement usually is not accompanied by pain until late in the course of the disease. As the tumor increases in size, symptoms of pressure are noted, such as nausea, vomiting, constipation, and shortness of breath which is caused by the upward displacement of the diaphragm. Anemia becomes a prominent symptom as the disease progresses. In the more serious cases, blood transfusions may be resorted to prior to surgical intervention. Symptoms referable to the urinary tract may be absent. The usual complaints are frequency, nocturia, hematuria, and burning on urination.

Renal neoplasms comprise about 20 per cent of new growths occurring in children. The age incidence is variably placed between 6 months and 6 years. There have been 17 instances of this neoplasm at the Cleveland Clinic, of which this patient is a typical example. In our series of 17 cases, there were 6 male and 11 female children.

Concerning the symptomatology in the series, 65.5 per cent of the cases exhibited an abdominal tumor, 18.7 per cent experienced nephritic or abdominal pain, 12.5 per cent had gross hematuria, and 23.0 per cent showed microscopic blood in the urine. An elevation in temperature was present in 25.0 per cent of the cases. Anorexia and loss of weight were protean throughout the series.

The diagnosis is made with little difficulty. The history given by the mother is suggestive. The initial roentgenogram may reveal a large mass in the region of the kidney. The diagnosis of a kidney tumor may be determined by the use of the intravenous urogram or retrograde pyelography. The pyelogram is most useful in arriving at a diagnosis, having established the diagnosis in 100 per cent of the cases in Kretsch-

mer's[8] series. The urogram is useful in only approximately 70 per cent of the cases. The reason for this is that a large amount of renal parenchyma may be destroyed, and there is insufficient renal tissue to concentrate the intravenous dye.

The accepted treatment at present is preoperative radiation therapy followed by nephrectomy. Kerr[9] advocates as preoperative radiation the use of 200 r units daily to each of three ports until a total dose of 3,000 to 4,000 r units have been given. He also advises the irradiation of pulmonary metastases. There are cases on record in which pulmonary metastases have disappeared following roentgen therapy. Some authors advocate the use of postoperative irradiation. Transfusion of blood may be required if pronounced anemia is present.

According to many authors the prognosis is not favorable. The mortality is variously placed at 90 per cent and very few patients have survived a five-year period. The most discouraging complication is metastases, the most frequent sites being first to lungs and second to bone. The duration of the tumor and the age of the patient seem to have little bearing upon the appearance of metastases.

As to the end results in our series, 9 patients were traced and all were dead with the exception of the one reported herein. The average duration of life, regardless of the therapy instituted, was 8.6 months. Nephrectomy was performed in 14 cases. Exploration was done in two cases, both of which were dead within a period of five months. There was no follow-up on 5 of the cases.

The morbidity and mortality in this group was as follows: 14.3 per cent lived two and one-half years, 21.4 per cent lived one and one-half years, and 69.0 per cent were dead within 6 months after operation.

## Conclusions

The case reported is a typical example of the occurrence of a Wilms' tumor in a child. The tumor was first noted by the mother, which is the usual rule. The primary symptoms were generalized, urological symptoms being secondary. There was no evidence of metastases to the pulmonary system or to bone.

This tumor was rapidly reduced in size by irradiation to each of three renal ports, a total of 5,100 r units being administered. Nephrectomy was then performed and roentgen therapy was instituted following surgical intervention.

The prognosis of this case is guarded. It is possible with pre- and postoperative irradiation combined with nephrectomy, that the patient may survive for the five-year period.

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# PREOPERATIVE CONSIDERATIONS OF THE JAUNDICED PATIENT

R. S. DINSMORE, M. D.

In the jaundiced patient, the surgeon must decide whether he is dealing with primary disease of the liver or biliary tract, with mechanical obstruction, or with a blood dyscrasia. He must remember that jaundice is but a symptom.

A careful history is extremely valuable. In addition to knowing whether the jaundice has been transient or persistent, a history of the presence or absence of pain, particularly in relation to the jaundice, is important. The symptom of pain has been the chief aid in making a diagnosis in a great number of the operative cases. In patients who have been operated upon previously, it is likewise important to know the nature and extent of the operation, and whether a cholecystectomy, cholecystostomy, or a choledochotomy has been done. In secondary operations the length of time the drainage persisted after the first operation, and the appearance of jaundice in relation to operation is of particular interest.

Jaundice was due to the presence of gall stones or associated lesions in 30 per cent of our cases. Hartman[1] states that 25 per cent of all cases of jaundice are due to gall stones or to complications from associated conditions, and 30 per cent to carcinoma, either primary or metastatic lesions which obstruct the biliary ducts. It is significant that in only 25 per cent of the cases in his series, including infectious and toxic cases, was the jaundice due to lesions of the liver parenchyma.

With these figures in mind, it must be concluded that even with conservative management exploration should be performed in well over one-half of all patients with jaundice. It is important to know whether the patient has been taking drugs of any kind, as a toxic hepatitis must always be considered since cincophen and similar drugs are so widely used.

Careful studies of the blood must always be made to rule out hemolytic jaundice. It should not be forgotten, however, that associated stones may be a complicating factor.

Unfortunately, cholecystography is contraindicated in patients with jaundice but roentgenologists have constantly stressed the importance of taking plain roentgenograms of the right upper quadrant, as gall stones frequently may be visualized. It also is important to take the roentgenograms at several penetrations while the bowels are completely evacuated.

Even with all the present means of diagnosis, some cases are seen in which it is necessary to perform an exploratory operation before a diag-

nosis can be made. Occasionally, a patient who comes in with what appears to be a hopeless malignancy will be found to have a stone impacted in the common duct.

Of particular importance is the degree of damage to the liver. Infection in the liver must be considered as an almost constant factor in obstruction caused by stones in the common duct.

The following points are of importance in the examination of these patients: (1) the function of the liver; (2) the coagulation time of the blood; (3) the level of the serum bilirubin; (4) studies of the renal function; (5) findings in the plain roentgenogram of the right upper quadrant; (6) the estimation of the prothrombin time; and (7) cholio-graphic studies if a secondary operation has been performed and a postoperative fistula is present.

It is known that patients with jaundice have a tendency to bleed after any operative procedure, but, as Mason[2] has stated, no test has yet been devised which can be relied upon to indicate that postoperative bleeding will not occur. Undoubtedly, the recent work of Butt, Snell and Osterberg[3] with the newly isolated vitamin K will be of distinct aid.

Although there is some controversy as to whether the lack of available calcium is one of the factors in the tendency to bleed, we still feel that calcium should be given as part of the preoperative routine. This has been emphasized by Lee and Vincent[4], Whipple[5] and particularly by Walters[6]. Five cc. of a 10 per cent solution of calcium lactate should be given each day during the entire preoperative period. Ordinarily, two transfusions of 650 to 750 cc. of blood are given. Following transfusions, a striking change always occurs in the appearance and general condition of these patients, and the coagulation time of the blood is lowered. In addition to the administration of calcium, blood transfusions and vitamin K, a large fluid intake is necessary, as dehydration must be borne in mind. The diet should be rich in carbohydrate. A 10 per cent solution of glucose in normal saline is given intravenously. Patients are encouraged to eat large quantities of hard candy.

Liver function tests are generally unsatisfactory. The liver has a large reserve, and often quite marked structural changes do not produce any alteration of function. The tests in use are: (1) the galactose tolerance test; (2) bromsulphthalein retention in plasma after intravenous injection; (3) Takata-Ara test of blood and ascitic fluid; (4) special studies to determine the volume and shape of the blood cells and the degree of anemia; and (5) determination of the total blood proteins.

The bromsulphthalein test is the most sensitive test now in use but is unsatisfactory in the presence of obstructive jaundice. The galactose tolerance test is not sensitive and has little practical application in

disease of the liver. The excretion of galactose may be impaired in jaundice caused by disease of the liver. If the jaundice is due to simple obstruction the test is normal.

The Takata-Ara test is positive in many types of disease of the liver. It is positive most frequently in cirrhosis. If there is ascites and the Takata-Ara test on the ascitic fluid is positive, the accumulation of fluid can usually be attributed to cirrhosis. These same observations are true in the determination of total blood proteins.

Anemia is a common finding where there has been damage to the liver. The red cell is nearly always larger than normal, so a macrocytosis of the red cells is suggestive of disease of the liver parenchyma. If there is obstructive jaundice, a flattening of the red cells occurs without an increase in volume. A change in the red cells seems to be the most sensitive index of liver function but studies must be repeated frequently to be of clinical significance. The most useful test is the bromsulphthalein test. The Takata-Ara test is simply done and may give valuable information.

The various methods for determining the coagulation time in severely jaundiced patients have always caused confusion. We have discarded all stab and puncture methods. They have proved unreliable, due to the fact that the blood has been expressed through the tissues. The Lee and White[7] method is used routinely. Five cc. of venous blood are withdrawn and 1 cc. each placed in five 8 mm. test tubes. The first tube is tipped at 4 minutes and the others at the same interval. If coagulation is not complete in 5 to 8 minutes, it is considered abnormal, thus giving an accurate coagulation time. The estimation of the bleeding time has not been of much clinical value in our hands.

In individuals who have had previous operations on the gallbladder or biliary duct and jaundice and a fistula have occurred, cholangiographic studies are oftentimes of great help in making a diagnosis. Many articles have been written on this subject. Best and Hicken[8] have particularly emphasized the use of cholangiography either as an immediate procedure at the time of operation, while a T-tube is in place, or where there is a persistent postoperative fistula. They also emphasized its importance at the time of operation, pointing out that many of the failures which follow short-circuiting operations or cholecystostomy have been due to occlusion of the cystic duct. There is no reason, however, why this should be used routinely in uncomplicated cases. If, however, a cholangiogram can be taken on the operating table, and the opaque substance is found to pass into the gastro-intestinal tract without obstruction, the abdomen can be closed with the assurance of patency of the common duct. Where a T-tube has been left for drainage, it is also of advantage to inject the opaque substance through the tube before it is removed.

From this general discussion, it must be concluded that these patients can no longer be sent into the hospital for emergency operations. If a low mortality rate is to be maintained, they must be prepared carefully for operation. Proper preparation has undoubtedly been far more important than any changes in operative technic. Preoperative preparation ordinarily requires from four to seven days and, as a rule, even if the patient is improving, it is better to extend this time rather than to shorten it.

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# THE DIAGNOSIS OF FOREIGN BODIES IN THE LOWER AIR PASSAGES

H. S. VAN ORDSTRAND, M. D.

The diagnosis of foreign bodies in the bronchi necessarily entails close correlation of an accurate history, physical examination, and stereoroentgenographic study of the lungs. It is often impossible to get a clear-cut history of something having been inhaled into the air passages, and the roentgenograms are occasionally misleading, especially in non-opaque foreign bodies. The purpose of this paper is to stress the diagnostic importance of a careful physical examination of the chest. The necessity of early diagnosis and removal in order to avoid complications such as abscess, bronchiectasis, and pulmonary gangrene is well known.

A positive history of a foreign body will be of the accidental entrance of some organic or inorganic substance into the trachea. Such a history may not be obtained, especially if the onset of symptoms is insidious. This is especially true in infants and very young children where a history of manipulating foreign matter about the upper respiratory tract cannot be obtained.

The manner of lodgment of the foreign body influences the symptoms to an important degree. This has been shown by the experimental work of Weinberg[1] who demonstrated the different degrees of pathological changes produced by vegetable and inert types of foreign bodies. He observed that obstruction caused by inhaled vegetable matter plays little part in the early disturbance of tissue. However, bronchial obstruction develops later and the tissue change which results is similar to that produced by obstructing inert foreign bodies. At this stage, the degree of obstruction rather than the composition of the foreign body determines the pathological changes in the lungs.

Roentgen studies are of value in demonstrating opaque bodies and evidence of obstructive emphysema. Iglauer[2] in 1911 and Manges, Jackson, and Spencer[3] in 1920, described the roentgenographic signs of obstructive emphysema. The first sign consists of increased transparency of the lung on the side the main bronchus is obstructed. This change is demonstrated during expiration. The diaphragm on the same side is depressed during expiration, while the heart and mediastinal structures are displaced toward the opposite side. However, these changes may not be observed on the roentgenograms or at fluoroscopic examination due to the rolling, ball-valve action of a potentially obstructing substance. As shown in one of our cases, the changes may be positive on one roentgenogram (Fig. 1) and negative on another a

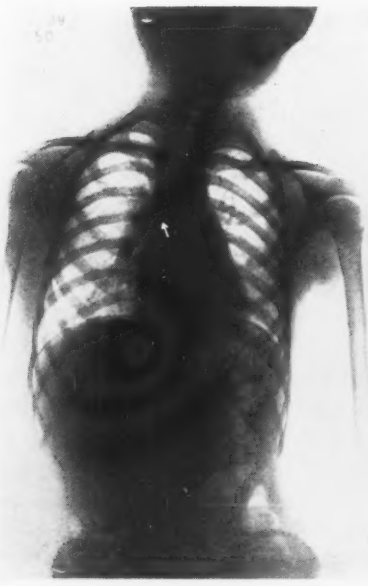

FIG. 1, (Case 1): Roentgenogram of the chest, taken in expiration, showing typical roentgen evidence of obstructive emphysema secondary to a foreign body (metal tip of whistle).

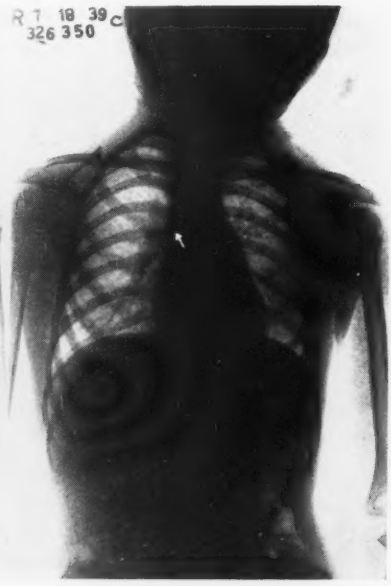


FIG. 2, (Case 1): Roentgenogram taken in different phase of respiration, showing typical roentgen evidence of foreign body in lower air passages, but not showing secondary roentgen changes of obstructive emphysema.

few moments later (Fig. 2). This case, on the other hand, demonstrates the helpfulness of stereoroentgenograms.

The findings on physical examination are of great importance in the diagnosis and localization of a foreign body in a bronchus; this is particularly true in the presence of non-opaque bodies. Inspection may show diminished expansion on the affected side. This is more marked in obstruction of an entire lung than in the unilobar type. Palpation is of aid in determining the site of the cardiac apical impulse as well as the decrease in tactile fremitus over the limits of the lung parenchyma supplied by the obstructed bronchus. A palpable rhonchus may or may not be present. Percussion usually elicits the so-called hypersonorous note over the involved part. Auscultation is usually the most helpful aspect of the physical examination and reveals diminished to absent breath sounds with decreased vocal fremitus over the involved area. Râles may or may not be found, depending on the type of foreign body and the interval between its lodgment and the time of examination. Other noteworthy features are the presence or absence of cyanosis, dyspnea, and stridor. Gerlings[4] stressed the findings in unilobar obstructive emphysema secondary to foreign bodies. These physical signs

are similar to those of an obstruction of a main stem bronchus, excepting that they conform with a single lobe pattern. Determination on physical examination is simple when one remembers the normal limits of the various lobes. This is difficult on roentgen study alone.

The following cases represent a foreign body of the metal group and vegetable family respectively.

*Case 1:* The patient was a girl four and one-half years of age who came to the Clinic on July 18, 1939. Two days previously, while blowing a whistle, the small metal tip had been aspirated. There were no immediate ill effects but a wheezing cough developed 24 hours later. No cyanosis was present and the temperature was normal. Wheezing with labored breathing was most marked when the child became excited.

*Physical Examination:* There was lessened expansion of the right side of the chest. An inspiratory rhonchus was palpable and audible over the entire chest, both anteriorly and posteriorly. It was strongest in the third right interspace near the sternum and just to the right of the fifth vertebral spine. The percussion note was hypersonorous over the entire right lung with decreased breath sounds. No crepitant râles were heard. Roentgen examination (Figs. 1, 2, 3) revealed increased transparency of the right side, depression of the right diaphragm, and displacement of the heart and mediastinal structures to the left. On expiration (Fig. 1), a circular, metal foreign body 1 cm. in size was seen at the level of the second right costosternal junction. A roentgenogram taken on inspiration (Fig. 2) and an oblique film (Fig. 3) did not help to localize the foreign body.

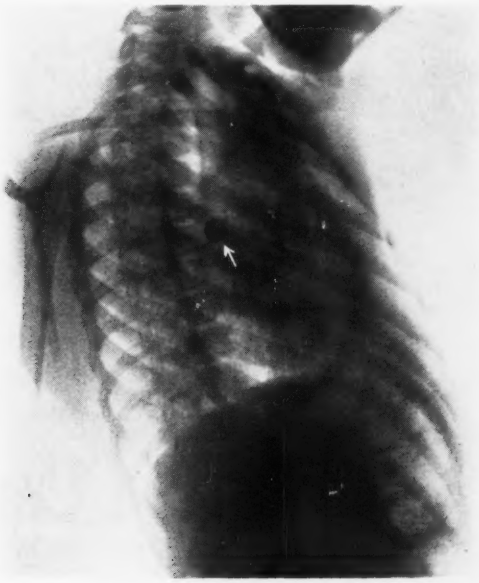

FIG. 3, (Case 1): Oblique film showing presence of foreign body but not localizing it.

A diagnosis of foreign body in the right main stem bronchus was made: Bronchoscopy was performed by Dr. Paul Moore and the metal disc was removed.

The postoperative course was uneventful. The cough subsided within 24 hours. The child has remained well.

*Case 2:* A boy, three years of age, came to the Clinic on July 5, 1939. The parents believed the child had aspirated a large peanut three days previously. Paroxysms of coughing developed immediately. There had been no previous cough and he had never had whooping cough or pertussis vaccine.

*Physical examination* revealed decreased expansion of the right lung with hypersonorous percussion note, right posteriorly from the third to ninth vertebral spine, and right anteriorly from the fourth to sixth rib. The breath sounds were suppressed to absent over the right lung in the same areas. Sibilant râles were heard at the left posterior apex, the first to third vertebral spine and anteriorly from the first to the fourth rib. The temperature was 99.6° F.

Roentgen examination of the chest was noncontributory.

A diagnosis of foreign body in the right main stem bronchus producing obstruction of the middle and lower lobes was made. Bronchoscopy was performed by Dr. Moore and half of a peanut was removed from this site. Little inflammatory reaction was noted about the area of lodgment. Following removal, the fever and cough subsided. A few crepitant râles in the right posterior hilar region persisted for 24 hours. The breath sounds and percussion note were normal. When last seen on July 12, 1939, the child had remained free from symptoms.

## Summary

The diagnosis of foreign bodies in the bronchi is made from the correlation of the history, roentgen examination and physical findings. The importance of a good physical examination is stressed from the standpoint of being a strong adjunct in diagnosis as well as its aid to the bronchoscopist in localizing the lodged foreign material.

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# THE CLINICAL SIGNIFICANCE OF AN INCREASED NONPROTEIN NITROGEN CONTENT OF THE BLOOD

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The nonprotein nitrogen of the blood exists in a number of heterogeneous compounds which are chiefly urea, amino acid, uric acid, creatinine, and creatine, and in a group of nitrogenous substances, the composition of which is little known and which are collectively spoken of as the undetermined nitrogen of the blood. Urea is quantitatively the most important component and, because of its ready solubility and diffusibility, it is distributed quite evenly between the cells and the plasma. The amino acids compose the next largest fraction and appear in greater concentration in the cells. Uric acid comprises only a small fraction of the total nonprotein nitrogen and is apparently evenly divided between the corpuscles and the plasma. Creatinine appears in small amounts in the plasma and in larger amounts in the corpuscles, and creatine is entirely confined to the cells. The undetermined nitrogen factor which comprises approximately one-third of the total nonprotein nitrogen in the blood is largely confined to the cells.

The total nonprotein nitrogen of normal whole blood ranges between 28 and 42 mg. per 100 cc. with an average of 32 mg. The urea nitrogen varies between 9 and 16 mg. per 100 cc. with an average of 12 mg. with urea values between 20 and 35 mg. The amino acid nitrogen varies between 6 and 8 mg. per 100 cc. with an average of 6 mg., and the undetermined nitrogen comprises between 10 and 18 mg. with an average of 14 mg. Uric acid determinations on normal blood range from 1.5 to 4 mg. per 100 cc. The normal concentration of creatinine in the blood is generally regarded as being from 1 to 2 mg. per 100 cc.

Concentration of the nonprotein nitrogen in the lymph in animals has been shown to be approximately the same as that of the blood serum both before and after bilateral nephrectomy. It has also been shown that the nonprotein nitrogen of transudates is approximately the same as that of the blood serum and this is also true with regard to synovial fluid. Spinal fluid, on the other hand, may contain considerably smaller amounts, partially due to the almost complete absence of uric acid. It has been shown that the various tissues of the body, particularly muscular tissue, contain greater concentrations of total nonprotein nitrogen than does the blood. It is believed that this excess nitrogen in the tissues is not held in simple diffusion but represents products of catabolism or anabolism of materials of more importance to the cellular economy. With an increase in the nonprotein nitrogen level

of the blood in nephritic conditions, it has been found that the pathological accumulation of nitrogen generally becomes distributed equally between the blood and the tissue but that the total nonprotein nitrogen content of the tissue still is higher than the nonprotein nitrogen in the blood. This excess of nonprotein nitrogen in the tissues over the nonprotein nitrogen in the blood is due to nitrogenous extractives, especially creatinine.

Theoretically, the nonprotein nitrogen level of the blood in the body at any time is dependent upon the amounts produced in the body in relation to the amount excreted through the various excretory channels. An increased production of any of the constituents could, therefore, cause an increase in the total amount. Actually, any considerable changes in the nonprotein nitrogen level are due to alterations of the concentration of urea or undetermined nitrogen, or both. Urea represents the chief end product of protein catabolism and under physiological and nearly all pathological conditions the values for urea and nonprotein nitrogen run parallel. The amino acid nitrogen in the blood is little affected by most physiological and pathological conditions and displays an amazing stability under various metabolic abnormalities, suggesting that there are regulatory mechanisms which provide a great margin of safety for this essential material. The greatest factor is apparently in the hepatic mechanism and only under conditions of severe damage to the liver do marked increases of amino acids occur in the blood.

The amount of uric acid in the blood is so small that even considerable fluctuations have little effect on the total nonprotein nitrogen and the same is true of creatine and creatinine. Creatinine increases in the terminal stages of renal failure only when the blood urea is already elevated. The undetermined nitrogen factor also increases considerably in nephritis and other diseases that cause elevation of the total nonprotein nitrogen but usually less than the urea nitrogen. Consequently, the level of blood urea may be taken as an index of the nonprotein nitrogen level of the blood.

The other chief factor determining the nonprotein nitrogen level of the blood at any time is its rate of removal from the body. The chief channel for the excretion of nitrogen is the kidney. The normal kidney is able to concentrate the urea of approximately 80 cc. of blood into 1 cc. of urine. With reduction in renal efficiency, this power decreases and larger amounts of urine must be excreted in order to remove nitrogen from the body without an increase of its level in the blood. Diuresis thus may overcome renal inefficiency for a time but, even in nephritis, the limit beyond which diuresis no longer increases the excretion of urea seems to be about three liters a day. There is, of course, a certain amount of nitrogen excreted in the feces and in perspiration,

The nitrogen in the feces, however, is not catabolic nitrogen and it has been shown that it does not increase to any degree even in conditions that increase the nonprotein nitrogen content of the blood. It is increased in high protein feedings only when proteins that are not assimilable are taken, and in diarrhea where it is believed that the increased nitrogen in the feces represents secretions from the intestinal mucosa rather than an actual excretion from the body. The use of cathartics, therefore, in attempting to treat elevations of nonprotein nitrogen in the blood is illogical, particularly when it is remembered that the incident diarrhea with loss of fluids to the body may increase the factor of dehydration from which these patients so frequently suffer, thus tending to lessen the renal flow.

Perspiration contains a certain amount of urea and nonprotein nitrogen and, with profuse diaphoresis, the cutaneous excretion of nitrogen may be considerable but it is doubtful clinically whether this function is of much value in renal inefficiency. For all practical purposes, therefore, it may be assumed that excretion of nitrogenous metabolites depends entirely upon renal efficiency. Besides the actual renal epithelial activity, this implies an adequate urinary volume since oliguria may in itself produce failure of excretion of nitrogen in a normal kidney. It must be remembered that in nearly all clinical cases, disturbances of nonprotein nitrogen are due not to single factors but to combinations in varying degrees.

There are certain variations of nonprotein nitrogen levels which are of physiological origin. Thus, after a meal rich in protein, the nonprotein nitrogen level of the blood rises gradually, reaching a maximum within three to four hours, and subsequently falling to the original level. The excretion of nitrogen in the urine follows closely the changes in the blood. In renal inefficiency it has been shown that the maximum is not attained for a longer period and takes longer to return to the fasting level, thus simulating the changes in the glucose tolerance curve in diabetes. The postprandial rise is caused by the delivery to the blood of extra amounts of amino acid from protein digestion and of urea from protein catabolism. If large amounts of fluids have been taken with the food, it is possible that the diuresis which occurs may prevent any postprandial rise. Because of the influence of dietary proteins, determination of the blood urea is usually considered most correct when taken in the morning during the fasting state. However, it must be remembered that in many cases the blood urea will be found highest at this time presumably due to nocturnal oliguria. Physical exercise, especially with food and water deprivation, markedly increases nitro-

genous wastes in the blood and may increase nonprotein nitrogen levels but, if the urinary volume and renal efficiency are adequate, the rise is slight and transitory.

Certain endocrine dysfunctions tend to disturb the nonprotein nitrogen level although usually not to marked degrees. Hyperthyroidism increases the demands of the body for fuel and if this is not supplied with a high caloric intake, protein in the body is used in undue amounts, thus tending to increase the level of nitrogen in the blood. Increased renal activity in the presence of sufficient urinary volume will prevent any clinical increase under such circumstances unless there should be renal damage. After parathyroidectomy it has been shown that the nonprotein nitrogen in the blood and the nitrogen in the urine increase particularly during convulsions and, according to a paper published by Haden[1] some years ago, the rise of the nonprotein nitrogen level of the blood under such circumstances is almost entirely confined to the undetermined nitrogen fraction. With convulsions, of course, there is markedly increased production of nitrogenous metabolites from muscular activity. This is frequently seen in convulsions in uremia. The nonprotein nitrogen level of the blood is found to be elevated somewhat in the terminal stages of Addison's disease. In diabetes mellitus when carbohydrate metabolism is poorly carried on and secondary fat metabolism is affected, there is liable to be wasteful burning of protein tissue in order to supply energy, thus tending to increase the nitrogenous waste in the blood. With an accompanying renal lesion or dehydration, the nonprotein nitrogen level of the blood may rise considerably. This is especially evident in precoma but is usually prevented by the marked diuresis which is characteristic of the disease.

Disturbances of the liver affect the partition rather than the total concentration of nonprotein nitrogen in the blood and in urine. After total hepatectomy, amino acid nitrogen rises while the urea nitrogen falls because in the absence of the liver the organism loses the power to diaminize amino acids and to form urea. This is also true in the terminal phases of acute yellow atrophy, but it is recognized that the hepatic reserve prevents such a condition existing until just before death. In advanced cirrhosis of the liver, in some hepatic conditions requiring surgery, and in diseases of the gallbladder and ducts, the nonprotein nitrogen level of the blood is frequently elevated. It is unlikely that these accumulations of nitrogen are referable to hepatic injury. They are more likely to be related to disturbances of renal function, deficient urinary volume, or excessive breakdown of protein from associated conditions which will be discussed later.

Following severe hemorrhage, transitory increases of nonprotein nitrogen in the blood with blood urea readings up to 200 mg. per 100 cc.

have been noted which have been shown to be unrelated to the anemia itself, inasmuch as they are corrected long before the blood elements have been restored. This may well be related to shock where fluid is lost from the blood and concentration of the blood occurs. Dehydration following hemorrhage certainly appears to be a factor in this increase. There is also the question of increased protein metabolism from the absorption of blood from the bowel. It has also been repeatedly shown that where plasma proteins are markedly decreased, the endogenous protein catabolism is increased. Then, too, it has been shown that the nonprotein nitrogen content of the tissue fluids is somewhat higher than that of the blood. Thus, when the blood volume is formed from the tissue fluids, the tendency may be to increase somewhat the nonprotein nitrogen level. This is in accord with the well-known fact that after venesection for uremia the nonprotein nitrogen level is usually higher than before venesection.

Borst[2], in a discussion of the basis for the increase in nonprotein nitrogen level following gastro-intestinal hemorrhage, states that the azotemia is usually associated with a hyperchloremia and a reduced excretion of urinary chloride. He cites the increased catabolism of body proteins in such patients when they are insufficiently fed, as well as the increased formation of urea from the blood in the intestines, and points out that the azotemia in itself results in a relative polyuria with maximal concentration of urea in the urine which may tend to restore the normal level. If, however, there is dehydration or shock from operation, the output of urine is decreased and the blood urea tends to rise. The post-hemorrhagic dilution of blood and consequent reduction of nonprotein nitrogen is retarded not only by the diuresis mentioned above and the restriction of intake of fluids which these patients usually undergo, but also by the low albumin content of the plasma following severe hemorrhage which lessens the power of the blood to draw fluid from the tissue spaces, and by the capillary damage associated with shock which readily allows fluid to leak from the vessels. It has been shown that sodium and chloride are retained when post-hemorrhagic dilution is in progress, while an increased excretion of potassium in the urine is observed. This is regarded as part of a mechanism established for the purpose of restoring the normal filling of the arterial system by way of an augmentation of the total extracellular fluid and therefore the blood plasma.

In the febrile stage of most acute infectious diseases, both the total metabolism and the nitrogen metabolism are considerably increased.

The loss of nitrogen in the urine cannot be entirely overcome by increased caloric feeding and it is concluded therefore that the greater protein catabolism in febrile infection is due not only to increased energy requirements but also to an active destruction of tissue. This toxic destruction of protein can be lessened but not abolished by the administration of sufficient fat and carbohydrates to provide for the energy requirements. The toxemia is somewhat parallel to the pyrexia and, of course, with high fever it is impossible to make patients who are ill consume sufficient calories. There is, therefore, a definite tendency for nitrogen catabolism to increase in the presence of fever due to this so-called destruction of proteins which is regarded as being due to an actual autolysis of tissue. The extra nitrogen appears in the urine in the form of urea plus ammonia, with some observers claiming also that excretion of amino acid rises under similar circumstances. If there is an accompanying renal lesion or an oliguria, it is evident that there will soon be an increase in the nonprotein nitrogen in the blood. This condition is very frequently seen in lobar pneumonia and may be regarded as being of some prognostic significance. There is always the question of an accompanying renal lesion, but it is likely that with normal kidney function a moderate elevation in protein catabolism and nonprotein nitrogen in the blood is frequently observed in severe pneumonia. It usually does not reach levels more than double the ordinary normal level unless there is definite renal damage. The value of the ingestion of large amounts of fluid in such cases becomes apparent inasmuch as it provides a vehicle for the excretion of the waste products and tends to restore normal values in the blood. Studies of urinary nitrogen under such circumstances frequently show large amounts of from 16 to 22 gm. per liter which in itself is evidence of efficient renal function, and also evidence of markedly increased nitrogen catabolism within the body. Haden[3] believes that the retention of nonprotein nitrogen in pneumonia is a toxic manifestation associated with the low serum chlorides so characteristic of the disease and he feels that the administration of sodium chloride has a specific beneficial effect—alleviating symptoms and diminishing retention of nitrogen. Van Slyke[4], however, believes that the effect of salt solutions is chiefly that of combatting dehydration and promoting diuresis.

It has been repeatedly shown that obstructions in the alimentary canal at any point from the esophagus to the rectum will cause an increased concentration of nonprotein nitrogen in the blood at times up to 300 mg. per 100 cc. According to some observers, the chief increase is in the undetermined nitrogen fraction rather than in urea. The earlier explanations of this phenomenon infer that the rises following intestinal obstruction were due to the absorption of toxic products of protein digestion from the obstructed loops of intestine, but it has been shown

that azotemia develops when the obstruction is at or above the pylorus, preventing the passage of protein to the intestine but not through it. Again the question of the efficiency of the kidneys has been raised, but it has been shown that under such circumstances, markedly increased amounts of nitrogen appeared in the urine and it has been shown frequently that the kidney can concentrate the urine to a high degree, even in spite of the oliguria and, in fact, may excrete abnormal amounts of nitrogen. It is, therefore, clear that the chief cause for the accumulation of nonprotein nitrogen in intestinal obstruction is due to an increased destruction of proteins and to some extent to dehydration. It has been well shown that such accumulation of nitrogen can be mitigated by the parenteral or rectal administration of sodium chloride solution.

In other surgical conditions of the abdomen, particularly associated with peritonitis, an azotemia is frequently seen. In this case a functional obstruction has occurred and the situation is aggravated by the dehydration from vomiting. The underlying infection probably plays a contributory role by adding to the protein destruction. Persistent vomiting in itself, even in the absence of obstruction of the alimentary tract, if sufficiently prolonged and severe to produce dehydration and starvation, will appreciably raise the nonprotein nitrogen level of the blood. Severe diarrhea, also, because of extreme water loss and dehydration, may be followed by an increase of the nonprotein nitrogen level of the blood, the effect being exaggerated by toxic destruction of nitrogen when associated with infection.

Uncomplicated heart failure may result in slightly increased nonprotein nitrogen levels of the blood, apparently due to a decrease in renal circulation and a relative oliguria. Digitalization in such cases may rapidly result in normal readings. Heart failure, however, complicating acute infection, may cause rapid accumulations of nitrogen in the blood and in nephritis the development of cardiac decompensation may cause it to rise rapidly. There seems to be a greater tendency to azotemia in syphilitic heart disease with decompensation perhaps because circulatory failure in this condition is a relatively late event. In hypertensive and arteriosclerotic heart disease with failure, increased nonprotein nitrogen levels are frequent, probably because of an associated sclerotic renal change. In bacterial endocarditis, a high nonprotein nitrogen content is a frequent occurrence and here the increased toxic destruction of protein associated with infection, as well as the renal lesions which may accompany the disease, probably afford an explanation.

The greatest elevations of nonprotein nitrogen levels of the blood which have been seen are those associated with some form of renal failure. The degenerative types of Bright's disease characterized by profuse albuminuria, renal edema, serum protein reduction, without

hematuria or significant hypertension, have shown an elevation of nonprotein nitrogen in the blood only in the terminal stages when renal failure supervenes, and usually in the presence of intercurrent infections which are likely to terminate the course of such a disease. The patient with degenerative Bright's disease has a tubular lesion and the difficulty is in regard to the water balance. The glomeruli are apt to be relatively normal and consequently no great difficulty is experienced in excreting the nitrogenous waste, provided an adequate urinary volume is arranged for. Such patients tolerate diets with high protein content well and may show positive nitrogen balances over a long period of time on a high protein intake, indicating a protein deficit undoubtedly caused by the albuminuria. As a matter of fact, the high protein diet increases the excretion of urea somewhat and this in itself tends to increase diuresis and lessen the edema. The administration of sufficient protein to cover the usual metabolic requirement, plus an additional amount to replace the loss of proteins as albumin in the urine, may be safely given without any danger of increasing the nitrogen in the blood. Even a considerable amount of additional protein may be given without danger because it is used for the restoration of wasted tissues. The high protein feedings which have been advised in this condition therefore have a rational basis, but it is often difficult to make these patients take diets containing 100 to 150 grams of protein daily. In these patients the actual administration of urea itself as a diuretic is often extremely beneficial and as much as 40 to 80 grams a day may be given without an increase of nonprotein nitrogen in the blood. Some transitory increase, indeed, may be noted but it is only by virtue of the fact that the urea does accumulate in the body to a certain extent that it gains its diuretic effect. It should, of course, be used with caution in the presence of azotemia and particularly if diuresis does not develop.

Accumulations of nitrogenous wastes are most apt to occur in those cases of Bright's disease characterized by persistent hematuria, hypertension, albuminuric retinitis, and eventually by the uremic syndrome. It is interesting to note that those patients who might be described as having a nephrotic type of chronic hemorrhagic Bright's disease characterized by edema and gross albuminuria are less likely to terminate in a state of uremia. Temporary elevations of the nonprotein nitrogen level of the blood are, of course, common in the acute phases of Bright's disease and may subside entirely with recovery of the renal state. Consequently, the actual level of the nonprotein nitrogen is of little prognostic significance in Bright's disease but much more important is the question of the direction which it is taking. In its inception, at least, acute hemorrhagic Bright's disease is often only a local expression of a general infection and this latter, by increasing nitrogen metabolism, may play

a considerable part in determining the extent of the accumulation of nonprotein nitrogen in the blood. The nonprotein nitrogen may rise in the presence of a comparatively high concentration of nitrogen in the urine and in negative nitrogen balance. The increase in these cases is usually due to a summation of the effects of impairment of renal function, insufficient urinary output, and increased nitrogen metabolism. In acute nephritis at times the rapid delivery of edema may result in a marked elevation of nonprotein nitrogen in the blood, the explanation of which is that the kidney apparently excretes the water much more readily than it does the nitrogenous waste which thus tends to be concentrated in the blood stream.

The highest elevations of nonprotein nitrogen noted have been seen in the end stages of chronic hemorrhagic Bright's disease. Retention occurs only when the renal function falls to a urea clearance value of approximately 20 per cent, although some elevation of the nonprotein nitrogen level of the blood may be noted with urea clearance values of 50 per cent or below. One patient seen recently at the Clinic was reported as showing a nonprotein nitrogen content of almost 600 mg. per 100 cc. Such elevations of the nitrogenous waste in chronic hemorrhagic Bright's disease are, of course, very serious unless there is some complicating factor such as heart failure which may help explain the rise as being due to some disturbance of renal circulation and not to an essential failure of the excretory function of the kidney. The fever which accompanies chronic hemorrhagic Bright's disease may aggravate the situation by causing a toxic destruction of body protein, but undoubtedly the biggest factor is the failure of the renal epithelium to secrete urea normally. By far the greater fraction of the elevation of the nitrogen in the blood is to be found in the urea portion. Uric acid, creatinine, and undetermined nitrogen are also elevated to a lesser degree, whereas amino acids and ammonia nitrogen are never significantly increased.

With the development of clinical uremia, some elevation of the nitrogenous waste in the blood is certain although this relationship to the clinical condition is extremely variable. Symptoms of uremia may develop while the nonprotein nitrogen in the blood is normal or only just above the normal limit and on the other hand may fail to appear even when the nonprotein nitrogen is extremely high. This variability is to be expected from the fact that neither urea nor any other known constituent of the nonprotein nitrogen appears to be responsible for the production of clinical uremia. As noted above, nonprotein nitrogen values as high as 300 mg. per 100 cc. have been noted in the blood of patients with longstanding pyloric obstruction without any symptoms of uremia and values almost as high have been noted in severe diarrhea.

Bollman and Mann[5], by implanting the ureters of dogs into the intestine so that the excretion of nitrogen in the urine was continually reabsorbed from the gut, have caused chronic increases of nitrogen in the blood urea amounting to more than 300 mg. per 100 cc. without the appearance of any symptoms of uremia.

Despite these apparent contradictions, the appearance of blood nonprotein nitrogen levels of 150 mg. or over are suggestive that uremia is not far distant, provided that elevation is due to disturbance of renal function. In the terminal stages of uremia the nonprotein nitrogen level of the blood may rise at tremendous rates, due partially to the fact that these patients become markedly dehydrated because of the inability to retain fluids and develop partial starvation. Further than this, the motor irritability and activity so characteristic of the state of uremia must increase caloric requirements and will increase protein catabolism when the ability to take fat and carbohydrate is limited.

In the arteriosclerotic kidney, accumulation of nitrogenous waste is less often seen because of the fact that the renal lesion is only part of a generalized vascular disease and renal failure is likely to be prevented by termination from cerebral vascular accident or myocardial failure. When renal failure does occur in this condition, the metabolic and chemical disturbances are indistinguishable from those found in chronic hemorrhagic Bright's disease.

Some elevation of the nonprotein nitrogen level of the blood is frequently seen in partial obstructions of the genito-urinary tract from prostatic hypertrophy or urethral stricture. The elevated nonprotein nitrogen may develop rather suddenly and reach levels as high as 200 mg. per 100 cc. It is rather characteristic of these increases that they are not accompanied by symptoms of uremia and with the relief of obstruction the normal level is quickly restored unless there has been underlying renal damage. Mass destruction of kidney substance from renal tumors, tuberculosis, pyelonephritis, hydronephrosis, pyonephrosis, and renal vessel thrombosis may result in markedly elevated nonprotein nitrogen levels of blood. Generally it is regarded that such an increase is suggestive of bilateral renal disease although cases have been reported in which the pathology was apparently unilateral. Such instances have usually been seen where one kidney was the seat of an infectious process and presumably the increased protein catabolism has overloaded the remaining kidney for the time being. It is frequently difficult to be certain that the remaining kidney is normal. Congenital polycystic kidney is a bilateral condition which is frequently responsible for a chronic type of increased nonprotein nitrogen level which may persist over years, during which the patient may carry on a normal activity. The renal reserve in such patients, however, is extremely small and a sudden excess strain upon the kidney, such as occurs with

a simple respiratory infection, may be sufficent to precipitate a marked further elevation of nitrogenous waste and death from renal failure. Blood urea levels of more than 100 mg. per 100 cc. certainly suggest that the patient is a poor operative risk at that time and indicates the necessity for conservative measures to relieve the obstruction or increase urinary output in order to secure more normal levels before radical operation is undertaken. Single determinations of the level of blood urea are not in themselves so significant but rather repeated checks should be made to determine its direction, particularly in relation to therapy.

Studies of the total urinary nitrogen are of great value in such conditions. If the excretion of the urinary nitrogen is greater than 8 grams per liter, it is presumptive evidence that the kidneys are damaged so little that provision of adequate volume of urine and reduction of protein catabolism may be expected to effect a considerable reduction in nonprotein nitrogen of the blood in these obstructive lesions as in the urea fraction when the urea may rise from its usual 50 per cent to comprise from 80 to 90 per cent of the total nitrogen of the blood. Uric acids and creatinine are less consistently affected while the undetermined nitrogen rises but to a lesser extent than urea. The ammonia and amino acid fractions alone appear to be entirely unaffected.

The marked elevation of one small fraction of the nonprotein nitrogen, namely uric acid, in acute attacks of gout is of considerable interest. The elevation of uric acid may occur without any appreciable elevation of the other fractions and there would appear to be some disturbance of the specific mechanism for metabolism of this constituent. Elevation of the total nonprotein nitrogen may be seen with acute attacks of gout but can be explained on the basis of the increased protein catabolism of the acute attack as well as the underlying renal lesion which so often occurs in these patients.

In summary it is apparent that the level of the blood nonprotein nitrogen at any given time is determined by the relationship of several different factors. These fall naturally into two important groups, namely, those which favor the increased production of nitrogenous wastes, chiefly protein catabolism, and those which favor their retention within the body, chiefly renal inefficiency. The largest fraction of nonprotein nitrogen in the blood is that contained in the urea and the greatest fluctuations are found in this constituent. The level of blood urea is usually used as an index of the relationship between the two main factions of the nonprotein nitrogen. Certain physiological variations of minor degree are noted. Major variations are of serious import and call for immediate therapy which depends upon the associated disturbances but mainly is concurred with a reduction of protein catabolism or increased urinary flow.

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# TULAREMIA TREATED WITH ARTIFICIAL FEVER THERAPY

*Report of a Case*

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When tularemia was first discovered, it appeared as though the occurrence of the infection was limited entirely to the Western part of the United States, but today it is found throughout the country. The causative organism is the bacterium tularense and the infection is non-contagious. It may be transmitted by any number of insects, but the usual source is the ordinary cottontail rabbit. An increased number of patients with this disease is seen during the hunting season because the infection is obtained from handling or skinning infected animals. This also explains the common site of the primary ulcer which is located most frequently on the fingers or the hand.

Netherton[1] described the primary lesion. The ulcer is granulomatous and the base shows a rich cellular infiltration with mononuclear cells predominating and a giant cell is noted occasionally. Marked hyperplasia of the endothelium of the capillaries is produced and in some areas the lumen is almost obliterated. Perivascular lymphatic infiltration at the margin of the lesion is especially noticeable.

The incubation period ranges from one to six days. The onset is usually sudden and is characterized by chills, headache, muscular pains throughout the entire body, especially in the muscles of the thighs and back, vomiting, prostration, and elevation of the temperature. The temperature usually ranges between 101° and 104° F. and continues to be high with some remission during the morning.

Tularemia is usually classified into four distinct clinical types: (1) ulceroglandular, (2) oculoglandular, (3) glandular, and (4) typhoid.

The ulceroglandular type is the most common. Francis[2] observed in 700 cases 80 per cent were in this group. Usually, about two days after a chill the patient notes an enlargement of the lymph nodes which drains the region of the site of the primary infection. The glands enlarge rapidly, usually out of proportion as is seen in other infections. They are distinctly painful and are connected by reddish-purple lines, indicating the presence of infection along the lymph channels. If the ulcer is on the hand, enlargement of the epitrochlear and axillary glands is noted, being marked in the former.

In the oculoglandular type, the infection is obtained by rubbing the eyes with infected fingers. This results in severe conjunctivitis and involvement of the pre-auricular parotids and submaxillary glands. The clinical picture will be described in more detail in the case to be reported.

In the glandular type, an adenopathy of the superficial lymph glands occurs but a primary lesion does not appear to be present.

In the typhoid type, the outstanding symptom is fever and enlargement of the spleen. No primary ulcer can be demonstrated and adenopathy is absent. The onset is the same as in the above types.

A positive diagnosis is made by obtaining an agglutination of bacterium tularense from blood serum collected in the second week of the illness and noting an increase in the agglutination titer in serum collected in the third week, or by isolation of the organism from the primary lesion, enlarged glands, or blood of the patient. The history is important and a diagnosis frequently can be made before the agglutination test is positive. The patient often gives a history of having dressed a wild rabbit or being bitten by a tick or fly. They usually have a primary lesion of the skin or conjunctivitis, persistent glandular enlargement in the region draining the primary lesion, and fever of several weeks' duration.

Foshay reported excellent results with specific serum[3]. Before this time treatment had been symptomatic. By the use of serum, he definitely reduced the convalescence, and improvement occurred within 24 to 48 hours after the injection was made.

The following case represents the oculoglandular type of tularemia. Serum therapy and local therapy also had been administered to the eye but there had been very little improvement.

## Case Report

The patient, a white housewife 53 years of age, had enjoyed good health until December 21, 1937, when stiffness in the muscles of the cervical region and nausea of a short duration was noticed. Three days previously she had cleaned a rabbit for Sunday dinner. The rabbit had been purchased at the market and was skinned. Five days after cleaning the rabbit the left eye became inflamed and pustular lesions appeared on the palmar surface of the middle finger and on the thumb of the right hand.

On December 28, 1937, the patient was seen in the Department of Ophthalmology by Dr. A. D. Ruedemann. Examination of the left eye showed conjunctival chemosis and swelling of the lids, which was more marked in the upper lid. There was moderate mucopurulent discharge. The palpebral conjunctiva of both lids was studded with yellowish spots. There also appeared to be some sloughing on the upper lid. The temperature was 101° F. Muscular soreness was marked.

From the history and clinical findings, tularemia was suspected. Smears and cultures from the left eye on December 28th showed nonhemolytic streptococcus and staphylococcus albus. Tularemia agglutination was negative. Agglutination was positive (1:80) six days later and was 1:10,240 on both January 10th and January 24th. Other laboratory findings were within normal limits with the exception of the sedimentation rate and Kahn test. The normal sedimentation rate by the Rourke and Ernstene[4] method is up to 0.45 mm. per minute

and this reading was 1.58 mm. per minute. The Kahn test was 2 plus on December 30, 1937, and negative on January 4, 1938.

Three injections of Foshay's tularemia serum were administered on January 10, 11, and 15, 1938. Generalized hives from the serum therapy developed on January 24th and lasted nearly two weeks. On February 18th, enlargement of the pre-auricular and submaxillary glands was noted. They became fluctuant ten days later and were incised and drained on March 7, 1938.

Very little improvement in the general condition and the condition of the eye was noted. On March 2, 1938, it was decided to give artificial fever therapy because some good results had been obtained by this method in the treatment of undulant fever. Artificial fever therapy was administered on March 4, 9, and 16, 1938. Each treatment was for five hours, the first up to 104° F. and the second and third to 105° F.

After the first artificial fever treatment the patient noticed marked improvement in the eye and it became progressively better following the successive fever treatments.

The patient has been seen at intervals and the eye is entirely quiet. When last seen on August 15, 1939, she was in good health and has had no recurrence. The tularemia agglutination at this time was positive (1:640).

Since just one case has been treated by this method, no deductions or conclusions can be made. It is reported merely because a good result was obtained and in the hope that it will stimulate other investigators to use this treatment when other therapeutic means have failed. Only after a large number of patients with tularemia have been treated by this method can its use be warranted.

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# THE VALUE OF PERIMETRY IN BRAIN LESIONS

R. J. KENNEDY, M. D.

The study of visual fields is one of the most important aids in the diagnosis of lesions of the central nervous system. The time and effort involved is well worth while as negative results are of value in excluding certain conditions.

Although the perimeter was introduced many years ago, before the ophthalmoscope, its greatest use has followed the stimulating work of Cushing and Walker[1]. They insisted on studies of the visual fields in every case where brain involvement was suspected.

Combined with pupillary changes, muscle paralysis or weakness producing diplopia with retinal lesion, and optic nerve involvement, the study of the visual fields is a valuable adjunct in many lesions in which the eye is directly or indirectly involved.

When the intracranial pathways are involved, the visual fields will indicate the approximate location and extent of involvement, but are not pathognomonic of the disease, although some definite inference can be drawn by progress studies.

Alteration of the visual fields must be considered as only part of the evidence upon which conclusions are based. It is the purpose of this paper to show that in several types of lesions, studies of the visual fields are not only an aid but, combined with encephalography and other neurological studies, are often of value in the diagnosis of certain lesions of the brain.

Perimetry is of value in the following types of cases[2]:

1. Cases in which the media is clear and the fundus is normal.

2. Cases in which ophthalmoscopic evidence is available, but further explanation is required.

3. Cases where disease of the retina or nerve path should be excluded or in which the media is partially obscured, interfering with satisfactory ophthalmoscopic examination.

Perimetry is especially valuable where visual impairment is apparently the only abnormality. The optic pathways with the site of lesions producing characteristic field defects is shown in figure 1.

Disease of the visual pathway in the region of the chiasm or posterior to it is characterized by changes in the visual field. This is known as anopsia. They are bilateral changes. The characteristic field defect resulting from chiasmal interference is known as bitemporal hemianopsia which, in its typical form, is found in tumor of the pituitary gland. Frequently, in cerebellar tumors, the third ventricle becomes so distended that it practically acts the same as a suprasellar tumor. Binasal

hemianopsia is due to pressure on each side of the chiasm; for example, in advanced sclerosis of the internal carotids. In diseases of the optic tract, complete hemianopsia is the rule. Homonymous hemianopsia may also be produced by tumors of the frontal lobe.

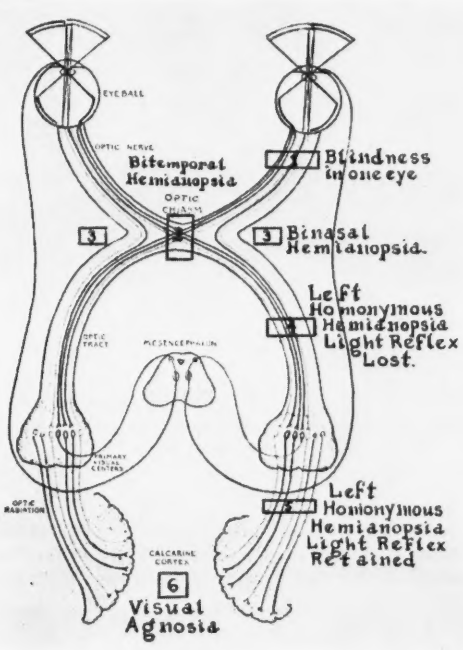


FIGURE 1: Diagram of visual pathway showing location of lesions which result in disturbances of vision. (Riley)

The following cases illustrate some of the more common visual fields findings and their relationship to encephalograms:

*Case 1:* A woman, 29 years of age, complained of pain behind the left eye. This began six months ago and was followed in one month by nocturnal attacks of jerking in the right leg. For two months there was weakness of the right leg. Examination of the fundus was normal. Study of the visual fields showed right superior quadrant anopsia, suggesting a lesion in the lower temporal lobe (Fig. 2). Vision in the right eye was 6/9 and in the left eye 6/6. An encephalogram was made which showed depression of the posterior part of the roof of the left ventricle, indicating that the tumor mass was near the vertex. A clinical diagnosis of a parasagittal meningioma was made and left frontoparietal craniotomy performed. The final diagnosis was glioma of the left motor cortex.

*Case 2:* The patient was a man, 30 years of age, who complained of headache, nausea and vomiting, and vertigo which had been present for 16 months. Examination of the fundus showed the right disc to be diffusely hazy

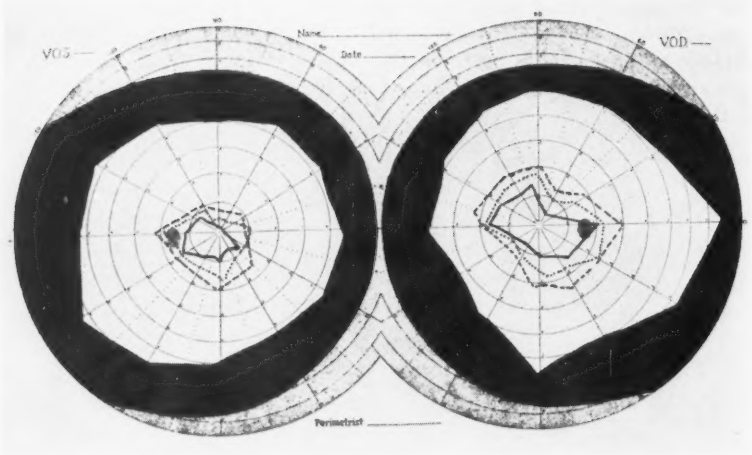


FIGURE 2: Right superior quadrant anopsia for colors in glioma of left motor cortex. (- - - - red, . . . . blue, ——— green.)

and left disc only slightly hazy. Vision in the right eye was 6/6-3 and in the left eye 6/9. Examination of the visual fields revealed left homonymous hemianopsia (Fig. 3). The encephalogram showed a tumor in the right temporal region. Operation was performed and a glioma of right lateral ventricle revealed.

*Case 3:* A man, 60 years of age, had had failing vision for 8 weeks, with loss of memory, confusion, and headaches. Examination of the fundus showed haziness and early edema of the optic discs, especially in the left eye.

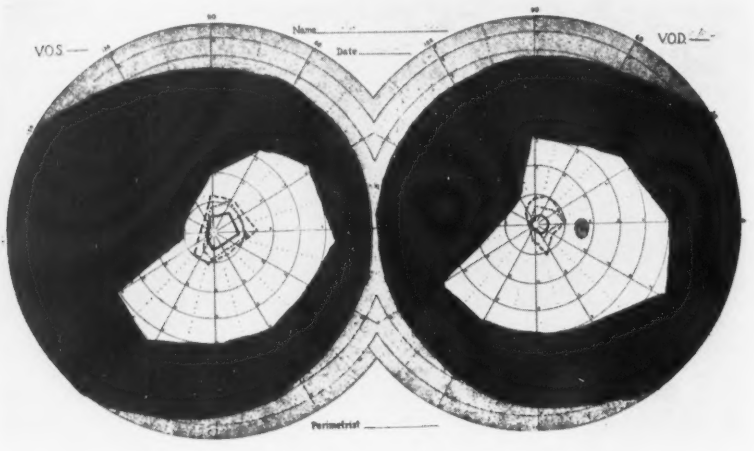


FIGURE 3: Left homonymous hemianopsia. Glioma right lateral ventricle. (- - - - red, . . . . blue.)

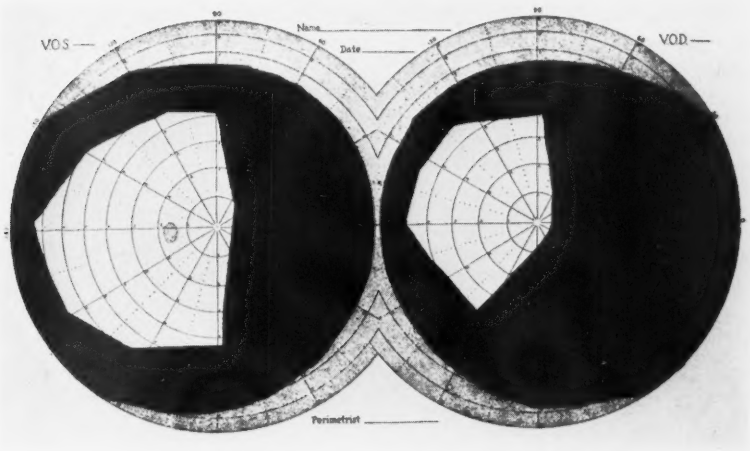


FIGURE 4: Right homonymous hemianopsia. Tumor of left frontal lobe.

Vision in each eye was 6/60. Examination of the visual fields showed right homonymous hemianopsia (Fig. 4). Encephalogram showed displacement of right lateral ventricle to the right. Operation was performed and a tumor of the left frontal lobe revealed.

*Case 4:* The patient was a man, 43 years of age, who had a history of headaches and changes in personality. Examination of the fundus showed 1 diopter of papilledema in each eye. Vision in each eye was 6/9. There was concentric contraction in both visual fields (Fig. 5). The encephalogram showed poor filling of the ventricles with displacement toward the right, suggesting a

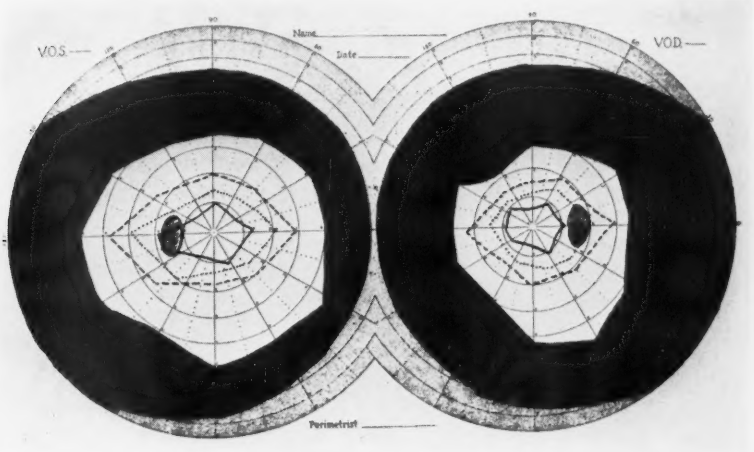


FIGURE 5: Concentric contraction. Glioma left frontal lobe. (- - - - red, . . . . blue, ——— green.)

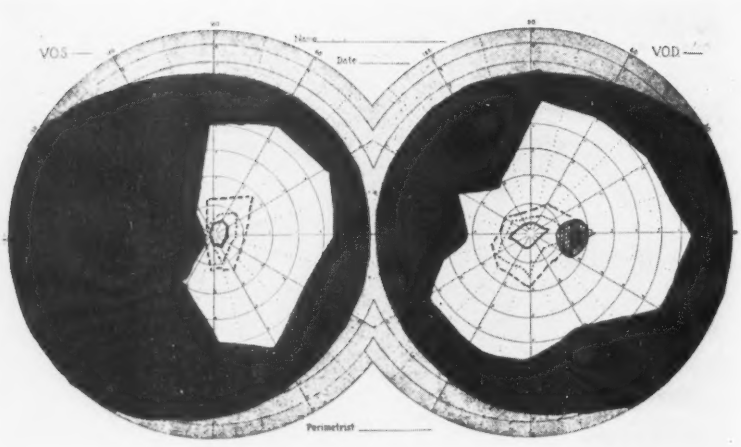


FIGURE 6: Left homonymous hemianopsia. Aneurysm of internal carotid. (- - - - red, . . . . blue, ——— green.)

space-filling defect of the left parietal area. A left frontal glioma was revealed at operation.

*Case 5:* A woman, 46 years of age, gave a history of failing vision in the left eye. A constant left-sided headache had been present for 6 months. She complained of weakness and 30 pounds in weight had been lost. Examination of the fundus showed slight haziness of the discs in both eyes, but no papilledema. Corrected vision in the right eye was 6/15 and in the left eye 6/6. Examination of the visual fields showed left homonymous hemianopsia (Fig. 6).

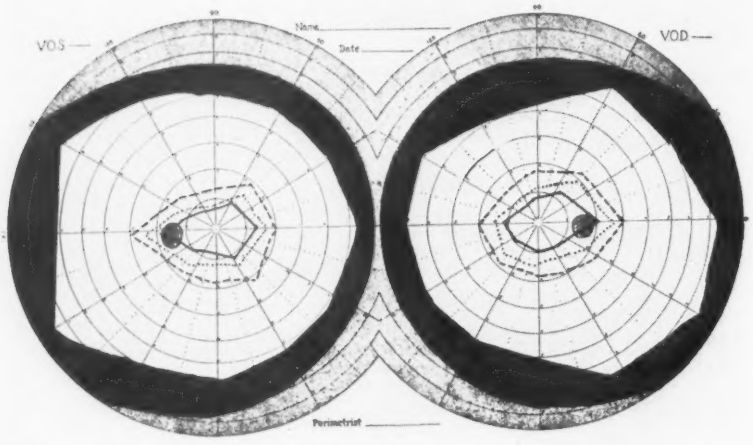


FIGURE 7: Essentially normal fields. Glioma right parietal lobe. (- - - - red, . . . . blue, ——— green.)

The encephalogram was negative. Operation revealed aneurysm of the internal carotid.

*Case 6:* The patient was a man, 33 years of age, who had had convulsions for 7 years. Examination of the fundus showed no papilledema and only slight haziness of the discs. The visual fields were normal (Fig. 7). Vision in the right eye was 6/5 and in the left eye 6/6. The encephalogram showed poor filling of the right lateral ventricle. A glioma of right parietal lobe was revealed at operation.

Table I shows nine cases of tumor of the frontal lobe; positive encephalograms were present in all of the cases. The visual fields are not diagnostic as to the location of the lesion.

TABLE I

*Visual Fields in Tumors of the Frontal Lobe*

9 CASES

| | |
|---|---|
| Concentric contraction | 5 |
| Enlarged blind spot, right eye | 1 |
| Right homonymous hemianopsia | 1 |
| Normal visual fields | 2 |
| Positive encephalograms | 9 |

## SUMMARY

Perimetry is of definite value as an adjunct to the diagnosis of intracranial lesions, but in itself usually is not sufficient. It is of definite aid in pituitary tumors but less exact in other lesions. Visual fields defects are sometimes difficult to explain, such as the right homonymous hemianopsia which occurred in the tumor of the frontal lobe in Case 3.

Generally speaking, perimetric fields give accurate and dependable information. At times they may be misleading, and we must look further for diagnosis. In such cases the encephalogram is of distinct advantage, combined, of course, with a good history and physical examination.

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# RHABDOMYOSARCOMA OF THE DIAPHRAGM

*Report of a Case*

E. J. RYAN, M. D.

The following case is presented because of the rarity of tumors primarily in the diaphragm, particularly those originating in voluntary muscle. Peery and Smith[1] reviewed the literature and reported a case in March of this year. Theirs was apparently the tenth case on record of a tumor primarily in the diaphragm, the sixth case of a malignant tumor, and the second case of such a tumor arising in voluntary muscle.

## CASE REPORT

A woman, 51 years of age, came to the Clinic in December, 1936, complaining of pain in the neck, fever, and abdominal distress. Two months previously she had had tonsillitis with peritonsillar abscess formation, and chills and fever. This was accompanied by sharp pain in the lower right posterior chest which was not influenced by respiration. Pain also developed in the posterior cervical area. It was constant at first, but was noted later only with a moderate rise in temperature which occurred each afternoon from the date of onset.

The gastro-intestinal symptoms consisted essentially of anorexia for two months, fairly constant nausea without vomiting, and intermittent abdominal distention for two weeks. She had lost seven pounds in weight.

Two ribs on the right side had been fractured a year previously, and a rib resection for empyema had been performed on the left side 18 years before.

Her mother and one aunt had died from carcinoma.

Physical examination on admission revealed weight, 144½ pounds, temperature 99.6° F., pulse 108 beats per minute, and blood pressure 155/78. No diaphragmatic descent with inspiration could be demonstrated on the right, although percussion note and breath sounds were normal. However, there was a definite coarse friction rub over the right posterior inferior chest.

A voided specimen of urine was negative except for 10-12 white cells per high power field. Examination of the blood showed 3,990,000 red cells with 65 per cent hemoglobin. There were 10,150 white cells with 84 per cent polymorphonuclears, 10 per cent eosinophils, 5 per cent lymphocytes, and 1 per cent monocytes. Blood urea and blood sugar were normal. Blood Wassermann and Kahn tests gave negative reactions.

Roentgen examination of the chest showed old fractured ribs in the lower right thorax, old resection of the eighth rib on the left side, and fibrosis in the left hilum.

The original examiner concluded that pus had collected above or below the right diaphragm, but exploratory thoracentesis was negative. Symptomatic therapy, rest, and high vitamin and caloric intake were prescribed and the patient was discharged.

Returning one month later, she complained of almost continuous nausea, anorexia, loss of weight, increasing weakness, and daily elevation of temperature. Physical findings were essentially the same as on her previous admission.

Examination of the urine showed 2+ albumin and an occasional cast. Blood count showed 4,170,000 red cells with 61 per cent hemoglobin, and 19,500 white cells with 69 per cent polymorphonuclears, 5 per cent eosinophils, 2 per cent

basophils, 15 per cent lymphocytes, and 9 per cent monocytes. Genito-urinary investigation, including intravenous urography, was negative. Roentgen examination of the chest showed a high right diaphragm with some lesion above or below it. Complete roentgen study of the gastro-intestinal tract was negative, except for a small irregularity in the pyloric region on the greater curvature, believed to be due to a band. Exploratory thoracentesis performed at this time was negative. Blood culture was negative.

In view of these findings, it was the consensus of opinion that a malignant process was present, and deep roentgen therapy to the retroperitoneal glands was suggested.

An exploratory laparotomy was performed on February 8, 1937. At operation, an excessive amount of free, serous fluid and numerous, small, fine adhesions were noted throughout the abdominal cavity and over the dome of the liver.

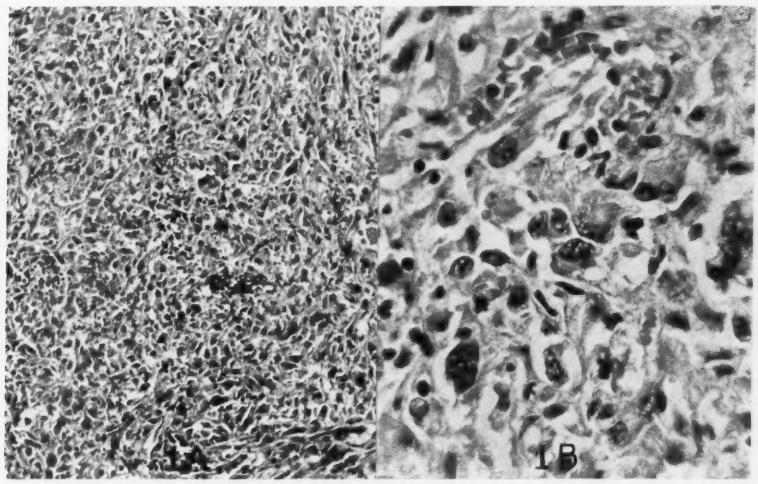


FIGURE 1: A.: Photomicrograph from pleural node. (x 150)
B.: Photomicrograph from pleural node. (x 600)

The gallbladder and appendix were removed, and pathologic examination revealed them to be chronically inflamed. Culture of the peritoneal fluid showed B. coli, B. alkaligenes fecalis, and nonhemolytic streptococcus.

The postoperative course was unsatisfactory. Parenteral fluids and frequent blood transfusions were necessary. The urinary output remained low and finally ceased. Urinary albumin varied from 2+ to 4+, edema appeared, the urea mounted and, on February 15, two days before her death, it was 198 mg. per 100 cc.

Necropsy showed a large tumor originating in the diaphragm and involving the liver, right pleura, and right lung by direct extension. The only distant metastases were in the peribronchial lymph nodes. The only other significant observations were diffuse acute pneumonia of the right lower lobe, generalized fibrinopurulent peritonitis, thrombosis of both renal veins, and degenerative changes in the tubular epithelium, with amyloid degeneration in many glomeruli. Micro-

scopic examination of the growth (Fig. 1) showed it to be composed of cells of variable size, shape, staining intensity, and nuclear content, with many gigantic tumor cells and multinucleated cells. In general, however, the cells were elongated, contained a large amount of pink-staining cytoplasm and oblong nuclei, and no recognizable longitudinal or cross striations.

It was the opinion of Dr. Allen Graham of the Department of Pathology, that the tumor represented a rhabdomyosarcoma, an opinion with which Dr. James Ewing concurred.

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# INTERSTITIAL CYSTITIS

WILLIAM J. ENGEL, M. D.

Although there are numerous reports in the literature dealing with the subject of interstitial cystitis, our experience justifies the statement that this disease is recognized too infrequently by the general profession, and that patients are too commonly subjected to diverse surgical attacks in a futile attempt to remove a most distressing pain, or even worse, they are classified as neurotics and denied proper investigation.

This disease was first described by Hunner in 1914, and therefore is frequently referred to as Hunner's ulcer, but it has also been termed submucous cystitis, panmural cystitis, elusive ulcer, etc. *Interstitial cystitis,* however, is a more descriptive title. Although originally described as a rare type of bladder ulcer, increased recognition has shown that it is not an infrequent lesion, and in the past fifteen years we have encountered 70 cases. It is preponderately a disease of females, 90 per cent of our cases having occurred in this sex. The majority appeared between the ages of 40 and 70, the extremes in our cases being 18 and 77 years of age. Of the 63 women, 10 were unmarried, while of the 53 who were married, 31 had borne children and 22 had not.

The etiology of this disease is quite unknown. In his original paper, Hunner suggested that focal infection might be the cause, and Bumpus and Meisser reported that they had reproduced the lesion in the bladders of rabbits injected with cultures obtained from the teeth and tonsils of patients suffering from the disease. Later, Moensch and Counsellor reported similar results using cultures obtained from the infected cervix of a patient suffering from the disease. They felt that, because of the preponderance of the lesion in females, infection in the cervix was a logical focus to explain the disease. However, the theory of focal infection has not been borne out in clinical experience and we have seen no patients cured by the removal of questionable foci. Others have felt that the disease was the result of previous attacks of cystitis, but in our group of cases no consistent history of antecedent inflammation of the bladder could be obtained. In only 12 cases was there any evidence of urinary infection at the time of examination at the Clinic.

Certain clinical and pathological features suggest that the bladder lesion is due to impaired circulation which might be caused by a vascular disease or nutritional deficiency. Whatever the cause, it would appear that it is part of a general process, the bladder lesion being only a local manifestation of the disease. In this connection, it is interesting to note that in one of our most severe cases there was also fibrosis and contraction of the sartorius muscle. Our ophthalmologist in examining the conjunctival capillaries in a few cases is of the impression that there is a diminution of the capillary bed.

In most instances one can almost make a diagnosis from a careful history. The long duration of symptoms is notable; in only three of our 70 cases had the symptoms been present less than a year and in one instance they had been present for 16 years. The chief complaint is frequent urination and the associated symptom is pain. In many instances the frequency is clock-like, it being necessary to empty the bladder at perfectly regular intervals, day and night. In certain cases the patients have related that they can almost tell the time at night by the regularity of the periods at which they have to arise. In this connection it is well to mention that nocturia is a *requisite* in the diagnosis, for without it the lesion does not exist, and this fact serves well in differentiating interstitial cystitis from other conditions producing diurnal frequency. The pain is usually suprapubic in the bladder area but may be in either lower quadrants of the abdomen, the groin, the vagina, perineum, or the rectum. It may be described as a knife-like pain or a burning distress, which reaches its maximum intensity when the bladder is distended with urine. Voiding usually brings temporary relief but the discomfort returns as soon as the bladder fills again. The pain is aggravated by motion, particularly jarring such as may be produced by riding in a motor car. Long years of suffering induces in these patients a severe nervous condition.

If the history contains the above features, one should always suspect interstitial cystitis. The frequent errors in diagnosis usually result from the fact that urinalysis in these cases is entirely negative and this tends to obscure the diagnosis. Equally confusing to the examining physician is the fact that very commonly, bimanual pelvic examination will reveal the presence of exquisite pain and tenderness to palpation, which may lead to a diagnosis of some type of pelvic disease for which operation is advised. It is interesting to observe that in 17 of our 70 patients previous operations on organs other than the bladder had been carried out without relief of the symptoms.

Although the diagnosis must finally be made by cystoscopic examination, it can be virtually established by introducing a catheter into the bladder and filling it to capacity. If this capacity is found to be small (less than 150 cc.) and if slight overdistention tends to reproduce the patient's pain, the diagnosis is presumptive, while if more vigorous overdistention is followed by a small amount of blood one may almost be certain of the diagnosis. These findings, of course, hold only for the typical case.

The cystoscopic picture is somewhat varied, but in general three types may be recognized: First, there may be early, diffuse involvement of the bladder without ulceration. In these cases one first observes that the capacity of the bladder is definitely limited. Careful examination fails to reveal any typical ulcer but one is impressed with the smooth

bladder mucosa which is unusually pale, and with the abnormal distribution of the vessels. The vessels in such cases are much shortened, having a fragmented appearance, and they seem to appear suddenly and then disappear with equal abruptness. Means terms this a pre-ulcer state but, although I have recognized this type in seven instances, I have never seen one go on to the development of a typical ulcer.

The second type is that which presents the more or less typical single or multiple, discrete, linear ulcer. This is the most common type and 52 or 74.3 per cent of our cases fell into this group. The ulcer is frequently very small and may escape detection unless the cystoscopist is looking for it. It is always on the movable portion of the bladder and quite frequently on the dome in the vicinity of the air bubble. I have never seen an ulcer on the fixed portion of the bladder, and believe that it never occurs. The typical lesion is first brought to the attention by its rather characteristic salmon-pink color. On closer inspection, this area is found to have a rather puckered or contracted appearance, creating a minute ridge on the summit of which is a linear, superficial, so-called ulcer, which is frequently covered with a faint white exudate. Although occasionally single, most of our cases have presented two or more such lesions. When such areas are touched with a ureteral catheter, they are found to be exquisitely painful and the patient immediately recognizes it as the pain she has been suffering. Forceful distention of the bladder provokes a most characteristic superficial splitting of the mucous membrane, followed by a trickle of blood which arises from multiple pinpoint sources. Frequently these lesions will be found in a bladder which otherwise appears perfectly normal, while in many cases the unusual distribution of blood vessels previously described will be seen in the adjoining mucosa.

The third type is the late ulcerative and contracted stage which was present in eleven, or 15.7 per cent of our cases. In this type, the bladder capacity is so markedly reduced that frequently it is impossible to carry out cystoscopy without anesthesia. Even then, the introduction of perhaps 30 to 50 cc. of solution will precipitate so much bleeding that accurate visualization of the bladder may be impossible. In such cases the entire bladder is involved with multiple areas of ulceration and fibrosis. To me, this type presents the greatest difficulty in diagnosis and it must sometimes be made by exclusion.

In the differential diagnosis, one must consider tuberculous cystitis, early infiltrating carcinoma, and radium ulcer. Since infection of the upper urinary tract must be ruled out in all cases, it naturally follows that differentiation from tuberculosis offers no particular difficulty. Although rarely confused with carcinoma of the bladder, biopsy examination should be employed if any doubt exists. The lesion produced by application of radium to carcinoma of the cervix may closely resemble

interstitial cystitis, but a history of radium treatment solves this problem. Thus there is ordinarily no difficulty in making the diagnosis in the first two types, providing the examiner has considered it as a possibility. Although the third type presents more difficulty, careful study will rule out all other possibilities.

The pathological picture seen in this disease conforms rather accurately with the cystoscopic findings which have been outlined. The mucous membrane is thin or absent, the normal transitional epithelium having changed to a single layer of flattened or cuboidal cells and there may be a very slight depression at the site of the actual ulcer. There is loss of the capillary bed which causes the larger arterioles to stand out prominently, and these have increased thickening of their walls. There is markedly increased thickening and fibrosis of the submucosa, with actual sclerosis in certain areas, which may even extend into the muscular layer. In many cases there will be, in addition, some lymphocytic and plasma cell infiltration, especially around the blood vessels.

Many methods of treatment have been advocated for the relief of this disease. Among the nonsurgical procedures, I mention irrigation of the bladder with silver nitrate solution, hydrostatic distention of the bladder, local application of pure phenol, and fulguration of the ulcer. More recently, Folsom has reported some favorable results from the injection of absolute alcohol into the ulcer bearing area. Any one of these procedures may be expected to afford a certain amount of relief.

The vast majority of our patients have been treated by a combination of hydrostatic distention plus fulguration under anesthesia. I feel that deep coagulation and extensive destruction of tissue is inadvisable and it has therefore been my practice to produce only the most superficial coagulation, using a large surface ball type of electrode. This is merely brushed over the ulcer in such a way as to produce only the most superficial blanching of the tissues. When this has been done, one notes a definite increased redness of the surrounding tissues with dilatation of the vessels. I believe the beneficial results are due to this increased vascularity stimulated by the lightest fulguration. The immediate result of this treatment is often miraculous, for even on recovering from the anesthesia the patient may express herself as feeling relieved and passes the first night in many months without arising to void. Recurrence of symptoms, however, is unfortunately the rule, the intervals of comfort ranging from three months to a year. In only three cases have I effected a cure as judged by relief of symptoms and disappearance of the ulcer, but all patients have been improved and the relief is so gratifying that they are satisfied to report every three to six months for repetition of the treatment.

Among the surgical procedures advocated are partial resection of the bladder, pre-sacral nerve resection, and ureteral transplantation. Hunner

originally advised resection of the ulcer bearing area of the bladder but later reported a high recurrence. This coincides with our experience, for we resected the ulcer in five cases with recurrence of symptoms in all instances. I believe this operation has been rather generally discarded.

Pre-sacral nerve resection, based on good theoretical principles, has yielded very disappointing results. Learmonth and Braasch reported the results of this operation for certain diseases of the bladder, eight operations having been done for interstitial cystitis. They considered only one patient cured and this one had, in addition, a resection of the ulcer. Quinby reported no relief in three patients in whom he resected the pre-sacral nerve. We have not performed this operation, but in two patients we have injected the paravertebral sympathetic chain. Although both patients obtained physiological effects as measured by increased temperature in the extremities, neither had the slightest relief of bladder symptoms. These facts constitute the chief argument against the conception that this is a primary vascular disease, especially one of the vasospastic type.

Ureteral transplantation should be considered a last resort, and should not be advised until one has exhausted more conservative efforts. It is indicated only in type three, where there is extensive ulceration and contraction of the bladder. We have carried out this operation on five patients, and the two who survived the operation have been entirely comfortable and happy, both regretting that they did not have it done sooner. No better statement of the indication for the operation could be given than a brief history of one of these patients.

A woman, 42 years of age, presented herself at the Clinic in April, 1931, complaining of having to void every 15 to 20 minutes; this was associated with suprapubic pain. She had had a hysterectomy without relief, and extensive bladder treatments with only slight temporary improvement. Examination showed a very nervous, undernourished woman, whose bladder capacity was 60 cc. Cystoscopic examination revealed a generalized ulceration and contraction of the bladder, which bled freely with overdistention. The upper urinary tract was normal. Treatment over a period of several months with distention and fulguration produced only meager results, the greatest capacity of the bladder being four ounces. It is difficult to describe this patient's misery, but suffice it to say that at times life was almost intolerable. We suggested to her the possibility of ureteral transplantation but she had planned a trip to Scotland and wished to postpone operation, so in a period of relative comfort she started her trip. On arrival in New York, however, her symptoms became very intense, and she consulted a surgeon who admitted her to the hospital and did a unilateral nephrostomy, advising that the other side be done later. This was not done, however, and insisting on her trip, the patient sailed from New York with a nephrostomy drain-

age. On arrival in Scotland, she consulted a physician who treated her for a time, and then she consulted a urologist in Edinburgh who advised and carried out a resection of the pre-sacral nerve. In the meantime, the kidney incision had healed, but she derived no benefit from the nerve resection and eventually returned to this country with bladder symptoms as bad as ever. By this time she was willing and anxious to have ureteral transplantation, which was carried out in November, 1933. This was done as a two stage operation, the patient having an entirely uneventful convalescence. She is still well at this date.

This is, of course, an extreme example, and yet it serves well to illustrate the type of case in which we have recommended ureteral transplantation. There are others among the ten cases in type three who should have it done but who have as yet been unwilling to accept the operation.

We have not deemed it necessary to do cystectomy, and this has not been done in any of our patients with ureteral transplantation. With the urinary stream diverted, the bladder becomes a nonfunctioning organ and no symptoms of the disease persist even though the bladder is still present.

# INTRATHORACIC GOITER

GEORGE CRILE, JR., M. D.

## INCIDENCE

Although many large goiters dip beneath the clavicles for a short distance, true intrathoracic goiters with extension downward as far as the arch of the aorta are relatively rare. In a series of thyroidectomies performed on 11,800 patients at the Cleveland Clinic Hospital there were only 97 cases in which the goiter descended to the arch of the aorta or below it, an incidence of less than 1 per cent.

## PATHOLOGY

It is a safe rule to consider all intrathoracic goiters to be adenomas originating in normally situated thyroid glands. All large intrathoracic goiters are adenomatous; in no instance in this series did a diffuse goiter descend to the arch of the aorta, and in all cases the adenomas had their origin in normally situated thyroid glands. We have seen several cases in which papillary adenomas arising in aberrant thyroid tissue and not connected with the thyroid itself were present in the superior mediastinum. However, these tumors are extremely rare and must be considered as a separate entity from the ordinary endemic goiter.

Intrathoracic goiter is a disease of the mid and latter span of life, the average age of the patients in this series being 53 years. The youngest patient was 32 years of age and in only 7 per cent of the cases were the patients under 40 years of age.

Since only adenomatous goiters become intrathoracic, it is not surprising to find the incidence of intrathoracic goiter highest in the older age groups in which adenomas are more common.

## ETIOLOGY

There is little doubt that the musculature of the neck plays a large part in directing the growth of an adenomatous goiter. Intrathoracic goiters as compared with other forms of endemic goiter are relatively more common in men than in women. They are also more commonly seen in stocky, short-necked individuals, in whom the pre-thyroid muscles are well developed. The pressure from these muscles tends to prevent the outward expansion of the goiter in the neck and gradually forces the adenoma downward into the superior mediastinum. Here for a time the adenoma may be freely movable, rising with deglutition or with straining, and descending again into the thorax. As the adenoma enlarges, it delivers from its intrathoracic position with less ease but still retains its attachment to the thyroid gland. Finally it becomes imprisoned in the thorax and continues to expand downward and laterally, the narrow thoracic outlet finally preventing its emergence into the neck.

## Symptoms

Patients with intrathoracic goiters may be divided, according to symptoms, into three groups: First, those with no symptoms; second, those with symptoms resulting from an associated hyperthyroidism; and third, those with symptoms resulting from pressure on the trachea and great vessels.

Large intrathoracic goiters are often completely symptomless and may appear entirely harmless. On the other hand very small intrathoracic goiters, situated in certain positions, may produce intolerable symptoms of pressure and tracheal obstruction.

The most severe symptoms occur in the cases in which the pressure of the enlarging adenoma is exerted exactly at the level of the thoracic out-

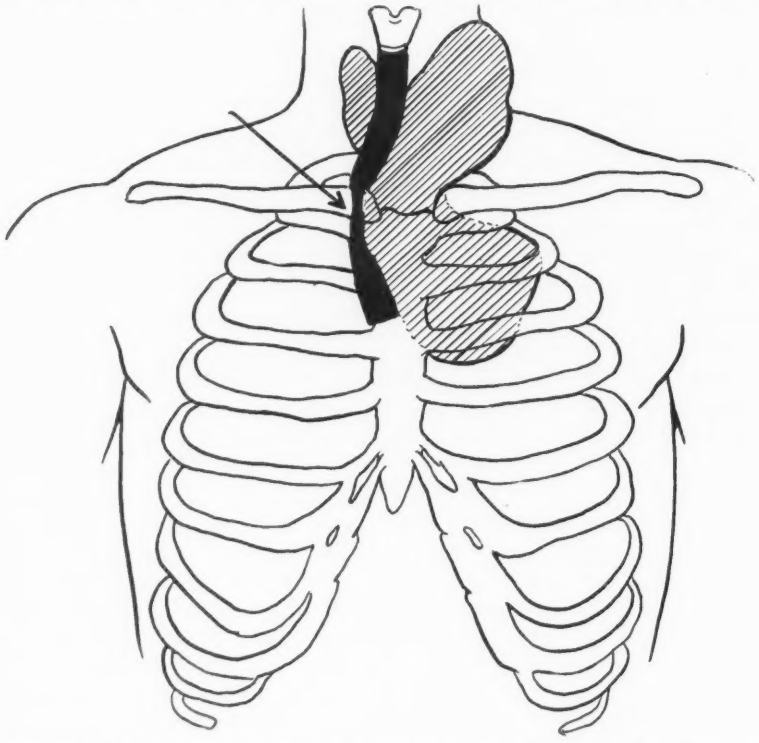

Figure 1: Arrow points to compression of trachea at level of thoracic outlet. Note that either flexing or extending the head would force larger portions of the dumbbell-shaped goiter through the narrow thoracic outlet and increase the pressure on the trachea.

let, the narrow and rigid bony structures at this level rendering it impossible for the tumor to expand without compressing the trachea.

The most common type of tracheal compression seen at this level is the

result of a dumbbell-shaped goiter, part of which lies above the thoracic outlet in the neck and the other part below the outlet and in the thorax (Fig. 1). The isthmus of the gland compresses the trachea between itself and the bony structures of the outlet and often results in severe symptoms of obstruction. To make matters still worse, extension of the neck, straining, or swallowing tends to lift the lower half of the dumbbell out of the thorax and through the contracted outlet, giving further pressure. Flexing of the neck, on the other hand, forces the cervical enlargement downward through the rigid outlet and again increases the symptoms of pressure. Hence, it is common for patients with intrathoracic goiter to complain that flexing or extending the neck, as in bending forward or in lying flat on the back, produces an unpleasant sensation of choking.

A second type of intrathoracic goiter which may produce obstruction of respiration is a relatively small adenoma located at the level of the thoracic outlet and situated either directly anterior to the trachea, compressing it backward against the vertebral column, or situated directly behind the trachea and compressing it forward against the sternum. The trachea may be considerably angulated and distorted by relatively small adenomas in these locations and the resulting symptoms of obstruction may be severe.

In contrast to the severe obstructive symptoms frequently experienced by patients with the above types of goiter, a high percentage of patients with large intrathoracic goiters—nearly 50 per cent in this series—had no symptoms referable to pressure or to tracheal obstruction. If the cervical portion of the thyroid is not enlarged sufficiently to result in fixation of the tumor, there is nothing to prevent an adenoma of the lower pole from growing downward into the thorax and expanding into the lung fields without producing symptoms of tracheal compression. In one case (Fig. 2) the entire upper lung field on the right was obliterated by an enormous intrathoracic goiter, which had expended its growth energy entirely by displacement of lung tissue. There was no compression of the trachea, and not the slightest symptom of pressure. The degree of tracheal obstruction will depend not so much upon the size of the tumor as upon its ability to expand without producing pressure on the trachea at the level of the thoracic inlet.

Hyperthyroidism was present in 50 per cent of all patients operated upon for large intrathoracic goiters and manifested itself in the usual way. In some cases it may be difficult to determine whether dyspnea, in a patient with an intrathoracic goiter, is the result of mechanical factors, the result of hyperthyroidism, or whether it is caused by primary cardiac disease.

The most common symptom associated with intrathoracic goiter is dyspnea, but in a high percentage of cases the dyspnea is secondary to an

associated hyperthyroidism or is the result of myocardial changes incidental to advancing age. In about 50 per cent of the cases, dyspnea was

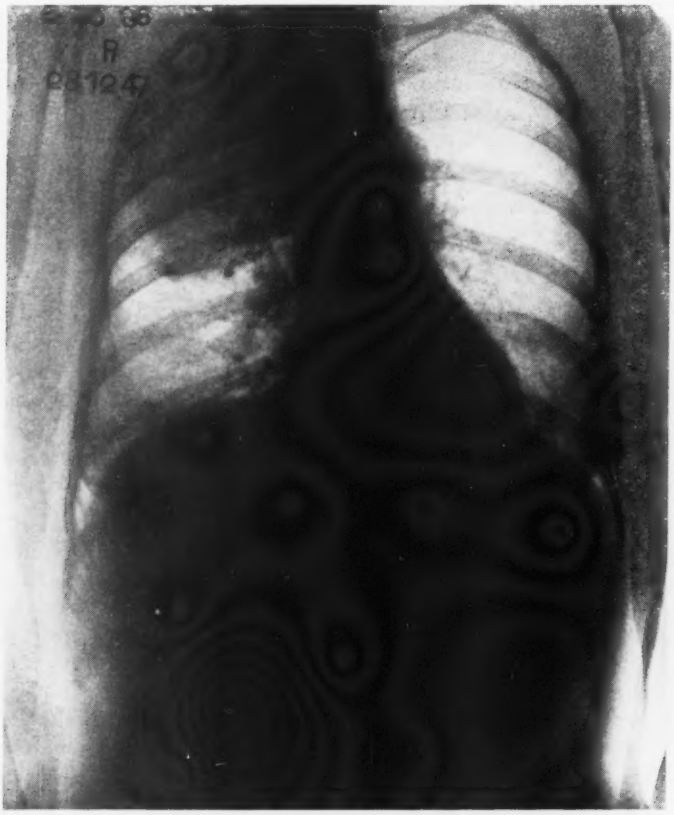

FIGURE 2: The entire upper lung field on the right is obliterated by an enormous intrathoracic goiter which had expended its growth energy entirely by displacement of lung tissue. There was no compression of the trachea and no symptoms of pressure.

a leading complaint and could not be explained solely on the basis of hyperthyroidism or myocardial damage. This symptom was completely relieved by operation in the great majority of these cases.

In 27 per cent of the cases the patients complained of choking sensations usually brought on by swallowing or by extending or sharply flexing the neck. The presence of this symptom is extremely helpful, as it is a certain indication that symptoms of obstruction are either present or are impending.

A late and specific symptom of tracheal obstruction is the development of stridor. This was noted in only 12 per cent of the cases. It is

characteristic of the stridor associated with intrathoracic goiter in that it occurs only when the patient is in certain positions, and most commonly during sleep.

Cough is rare and frequently represents a late symptom of intrathoracic goiter. When present it is often of a peculiar brassy quality. As a rule, however, there is little irritation of the trachea even when a moderate degree of compression is present. In severe cases, longstanding obstruction of the trachea may result in bronchiectasis, which signifies its presence by a productive cough.

Dysphagia, resulting from pressure on the esophagus, is rare and did not occur in any case in this series.

A sense of pressure, occasionally so severe as to be classified as a substernal pain, may be produced by an intrathoracic goiter. In some cases it may be confused with angina pectoris if a careful analysis of the complaint is not made. This symptom is rare, and the relation of the pressure sensation to swallowing and to the position of the neck, rather than to excitement or exertion, are important points in relating the symptom to the presence of an intrathoracic goiter.

Hoarseness is rarely caused by an intrathoracic goiter. In only 2 per cent of this series (in all of which the goiter descended to the arch of the aorta or below) was there a preoperative paralysis of the recurrent laryngeal nerve. A change in the quality of the voice, secondary to distortion of the larynx and trachea, is more commonly seen, and in some instances difficulty in singing occurs.

In spite of the fact that severe symptoms of pressure, such as choking and stridor, are present in less than one-third of the cases, it is nevertheless true that many patients who have no complaints prior to operation will obtain striking improvement in their general sense of well being after the removal of a large intrathoracic goiter. In these cases, just as in the case of women in whom large symptomless fibroids of the uterus slowly develop, the pressure symptoms have come on so gradually that the patient accustoms himself to their presence, and scarcely realizes that they have been a burden until the tumor is removed. So, in the case of patients with large goiters, obscure sensations which they have come to accept as normal will disappear and leave the patient with a sense of well being that has not been experienced for years.

## Diagnosis of Intrathoracic Goiter

An intrathoracic goiter can easily be overlooked, and unless routine roentgenograms of the chest are taken a small number of cases will always escape recognition. Most intrathoracic goiters are palpable and can sometimes be percussed. The symptoms of tracheal obstruction or the presence of dilated veins over the thorax may indicate the presence of an intrathoracic goiter. But the final decision as to the nature and extent

of the mediastinal tumor usually depends upon the roentgen findings.

In the anteroposterior view of the chest the trachea can be seen to be compressed or displaced by a smooth shadow descending from the neck. As a rule, this shadow completely fills the area just below the thoracic inlet, and becomes narrower as it descends to meet the shadow of the aorta. As Nichols[1] has pointed out, the demonstration of an angle between the mediastinal tumor and the arch of the aorta differentiates an intrathoracic goiter from an aortic aneurysm. Under the fluoroscope, or by means of the chimograph, the absence of expansive pulsation and the tendency of the tumor to rise when the patient swallows will further distinguish an intrathoracic goiter from an aortic aneurysm. Finally, a lateral view is indispensable in demonstrating the relationship of the tumor to the trachea and in revealing small adenomas compressing or displacing the trachea from in front or from behind.

## Treatment of Intrathoracic Goiter

The treatment of intrathoracic goiter is surgical. Roentgen therapy is utterly ineffective in reducing the size of an intrathoracic goiter or in alleviating the symptoms it produces. These tumors are well differentiated adenomas, are not sensitive to irradiation, and do not diminish in size in response to treatment with iodine.

When an intrathoracic goiter is large enough to descend to or below the arch of the aorta, its removal may present technical difficulties so the risk of thyroidectomy is considerably increased. Thus, in older patients who have large but symptomless intrathoracic goiters, it is not always wise to advise their removal. This is particularly true in patients over 65 years of age in whom life expectancy may be shortened by the presence of arteriosclerosis, hypertension, or myocardial damage. In such cases, if the goiter is not enlarging, if it is producing no symptoms, and if hyperthyroidism is not present, it is more than likely that the patient will die of other causes before the goiter produces any discomfort. But in younger patients, in patients with hyperthyroidism, and in patients in whom symptoms of obstruction are present, thyroidectomy must be performed unless strong contraindications are present.

## Technic

Since intrathoracic goiters are adenomas originating in normally situated thyroid glands, it is clear that the operation for intrathoracic goiter should be directed primarily toward the cervical portion of the tumor. The operation can be conveniently divided into five definite steps:

(1) The cervical portion of the thyroid is dissected free of its capsule of muscle and fascia.

(2) The superior pole is clamped and divided.

(3) The tracheal attachments of the thyroid are cut over hemostats whose points are always directed away from the tracheo-esophageal groove and into the thyroid tissue where there is no possibility of injury to the recurrent nerve.

Up to this point no direct attack on the intrathoracic portion of the gland has been made. With the cervical portion of the gland freed from the trachea, with the superior pole cut and tied, and with the isthmus of the gland divided, the intrathoracic portion tends spontaneously to slide upward into the incision.

(4) Gentle traction is made on the intrathoracic portion, using the cervical portion of the gland as a handle.

(5) As the gland delivers upward out of the thorax, it is carefully dissected free of its capsule. The lateral thyroid vein and the branches of the inferior thyroid vessels are then clamped, cut and tied as they present themselves in the field.

There is rarely any bleeding from adhesions or fibrous bands that may be present at the base of the intrathoracic extension. The operation should be practically bloodless if a careful dissection is performed and if the blood supply of the adenoma is meticulously ligated before making a forcible attempt to withdraw the intrathoracic extension.

The recurrent nerve is rarely displaced by an intrathoracic goiter except as it is pressed further medially into its normal position in the tracheo-esophageal groove. Hence, if the operation is performed gently, and if the capsule is dissected carefully as the gland is delivered into the wound, there is little danger of injury to the intrathoracic portion of the nerve. The greatest danger of nerve injury is at the point where the nerve comes forward to enter the larynx. Fixation of the intrathoracic portion of the goiter, as we have already mentioned, often renders it impossible to rotate the gland up from its bed. Dissection under these circumstances must be carried blindly downward along the side of the trachea, and this can be done with safety only if the points of the hemostats are always inserted into the thyroid tissue. Hemostats must be carefully applied, because if large bites are taken the ligatures may include the nerve and result in its paralysis. In small goiters, the gland can be rotated up into the field before it is liberated from the trachea, the lateral thyroid vein can be ligated and divided and the course of the recurrent nerve can be carefully avoided.

Collapse of the trachea probably never occurs except secondarily to bilateral injury to the recurrent nerves. The appearance of collapse is the result of strong inspiratory efforts in an attempt to suck air through the narrow chink between the paralyzed cords. The suction draws the walls of the trachea together and gives the appearance of spontaneous collapse.

Occasionally, during the delivery of a large adenoma, compression of the trachea will take place, but the normal shape of the trachea is restored as soon as the pressure is removed. Since force should not be used in delivering the goiter, this complication should rarely occur.

It is nearly always possible to remove an intrathoracic goiter without splitting the sternum or disturbing the bony outlet of the thorax. Splitting the sternum produces considerable shock and increases the incidence of postoperative pulmonary complications. This procedure should therefore be avoided if possible. In this series it was necessary to split the sternum in only one case and the outcome in this instance was fatal, the patient dying as the result of a mediastinal hemorrhage.

In all but three of the remaining 96 cases the goiter was removed through the usual cervical incision. In two of these three cases large cervical adenomas were removed with relief of the symptoms of pressure. In view of the patients' debilitated condition, and the technical difficulties involved, it was not thought to be advisable to attack the intrathoracic portion of the gland. In a third case, every effort was made to remove the intrathoracic portion but the lobes had extended bilaterally behind the trachea and into the mediastinum for a distance of 3 inches below the arch of the aorta. It was technically impossible to remove the tumor and matters were further complicated by the presence of advanced bronchiectasis which predisposed the patient to pneumonia and afforded a strong contraindication to splitting the sternum.

In all other cases (over 95 per cent of the total series) the entire tumor was removed through an ordinary goiter incision and without disturbing the bony structures of the thorax. In several cases the tumor was too large to be delivered intact through the thoracic outlet, but its complete removal was successfully accomplished by ligating the blood supply entering from above, opening the capsule of the adenoma, and then breaking up the tumor and removing it piecemeal. This procedure is accompanied by little or no bleeding and, after the removal of sufficient tissue, the capsule of the adenoma can be delivered through the thoracic outlet and excised. Bilateral extracapsular ligation of the main trunks of the inferior thyroid artery is of value in these cases whenever it is technically possible to do it.

There has been considerable controversy as to the treatment of the cavity left by removal of an intrathoracic goiter. Some have insisted that the cavity be packed open in order to control bleeding[2], wall off the cavity, and prevent mediastinal extravasation of blood or serum. This technic is unquestionably of value in the rare case in which there is persistent and uncontrollable oozing from the walls of the cavity. But in the great majority of cases, the cavity left by the removal of an intrathoracic goiter is merely a *potential* space and is quickly obliterated by the pleura and mediastinal tissues as they are forced into it by the intra-

thoracic pressure. By the use of packing, this potential space is transformed into a true cavity which is highly susceptible to infection and may drain for weeks.

In our hands the most satisfactory treatment of the mediastinal space has been closure without packing. Two or three small rubber drains are left in the cavity for several days to allow blood and serum to drain freely until the walls of the cavity fall together and become firm enough to prevent mediastinal extravasation. Better drainage is afforded by rubber than by gauze and the results with this method have been superior not only in respect to wound healing but also in respect to control of mediastinal extravasation. No fatal case of mediastinal hemorrhage has occurred since this technic was adopted some 5 years ago.

## Discussion

In this series of 97 cases, all of which were large intrathoracic goiters descending to or below the arch of the aorta, there were only two postoperative deaths in patients who did not have hyperthyroidism. The mortality rate from removal of these tumors, large though they may be, should not be high, provided the general condition of the patient is satisfactory.

When hyperthyroidism is associated with an intrathoracic goiter, the risk is definitely increased. If the patient is under 55 years of age, there is little danger whether hyperthyroidism is present or not. In the oldest age groups, when the patients are in the late sixties and seventies and have both hyperthyroidism and large intrathoracic goiters, the risk of operation is increased to about 20 per cent. It is thus clear that in older patients in whom active hyperthyroidism complicates an intrathoracic goiter, a certain amount of conservatism must be exercised in regard to the surgical treatment of the goiter.

Technical accidents, i.e., mediastinal hemorrhage, asphyxia, and infection have not been important causes of postoperative death. Three patients in this series, all cases operated in the early period in which the wounds were packed open with gauze, died as a result of mediastinal hemorrhage. There were no deaths from asphyxia or from mediastinitis.

Pneumonia was the most common single cause of death following operations for intrathoracic goiter. Other fatal complications in these elderly patients have been coronary occlusion and cerebral hemorrhage.

In view of the tendency to pulmonary complications, it is clear that general anesthesia with its attendant depression of the cough reflex and of cellular metabolism should be avoided. The operation can be performed under local anesthesia with no discomfort to the patient and with less risk of the necessity for an emergency tracheotomy. Intratracheal anesthesia is unnecessary and is actually undesirable because of its tendency to produce tracheal irritation and increase the amount of

mucus postoperatively. In addition, the use of intratracheal anesthesia necessitates deep narcosis with its attendant danger of pneumonia. In only two instances in this series was it necessary, because of respiratory obstruction, to perform a tracheotomy at the time of operation. These tracheotomies were promptly closed and convalescence was complicated by only slight infection in the wounds. If the operation is performed under local anesthesia, if the upper attachments of the goiter are completely freed, and if the goiter is delivered with extreme gentleness, there should rarely if ever be any obstruction to respiratory exchange.

## Summary

1. Large intrathoracic goiters are rare. Ninety-seven cases in which the tumor descended to or below the arch of the aorta are reported.

2. Intrathoracic goiters are almost invariably adenomas originating in a normally situated thyroid gland.

3. Large intrathoracic goiters may give no symptoms if their growth energy is directed toward displacement of lung tissue rather than toward compression of the trachea.

4. Compression of the trachea is most commonly seen at the level of the thoracic outlet.

5. It may be difficult in patients with intrathoracic goiter to differentiate among dyspnea due to organic heart disease, hyperthyroidism or tracheal compression.

6. Surgery is the only effective treatment for intrathoracic goiter.

7. The technic of operation is outlined.

8. The risk of operation is slight when the patient is not old or debilitated.

9. In patients over 65 years of age, in whom active hyperthyroidism is associated with an intrathoracic goiter, the risk of operation is considerably increased. In these cases, if the patients' general condition is not satisfactory, conservative therapy is justified.

## References

1. Nichols, B. H.: Personal communication.
2. Lahey, Frank: Intrathoracic goiter, S. Clin. North America, 16:1613-1629, (December 1936).

# The Frank E. Bunts Institute

The Frank E. Bunts Institute will present a course in General Diagnosis and Treatment on Monday, Tuesday, and Wednesday, November 13, 14, and 15, 1939.

The program of the course and an application blank will be found on succeeding pages of this Quarterly.

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## PROGRAM

## GENERAL DIAGNOSIS AND TREATMENT

### Monday, November 13, 1939

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|---|---|---|
| 8:00 A. M.— 9:00 A. M. | Registration | |
| 9:00 A. M. | Welcome | GEORGE CRILE, M. D. |
| 9:00 A. M.— 9:45 A. M. | Diagnosis and Treatment of Acute Syphilis | E. W. NETHERTON, M. D. |
| 9:45 A. M.—10:30 A. M. | Infection of the Head—Brain Abscess—Otitic Meningitis | W. J. GARDNER, M. D. |
| 10:30 A. M.—11:15 A. M. | Conservative Measures in Genito-Urinary Surgery | W. E. LOWER, M. D. |
| 11:15 A. M.—12:00 Noon | Diagnostic Bronchoscopy | PAUL M. MOORE, M. D. |
| 12:00 Noon— 1:00 P. M. | Luncheon | |
| 1:00 P. M.— 2:00 P. M. | Demonstration of Patients—Surgical Treatment of Hypertension | GEORGE CRILE, M. D. |
| 2:00 P. M.— 2:45 P. M. | Contact and Atopic Dermatitis | GEO. H. CURTIS, M. D. |
| 2:45 P. M.— 3:15 P. M. | The Investigation of the Allergic Patient | C. R. K. JOHNSTON, M. D. |
| 3:15 P. M.— 4:00 P. M. | Disturbances of the Knee Joints and Their Treatment | J. A. DICKSON, M. D. |
| 4:00 P. M.— 4:45 P. M. | The Diagnostic Value and Limitation of Intravenous Urography | W. J. ENGEL, M. D. |
| 6:00 P. M. | Dinner | |
| 8:00 P. M. | Frank E. Bunts Lecture | FRANCIS BENEDICT, M. D. |

## Tuesday, November 14, 1939

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| 9:00 A. M.— 9:45 A. M. | The Principles of Management of Late Syphilis | E. W. NETHERTON, M. D. |
| 9:45 A. M.—10:30 A. M. | Clinical Significance of Hematuria | C. C. HIGGINS, M. D. |
| 10:30 A. M.—11:15 A. M. | Treatment of Chronic Ulcerative Colitis | E. N. COLLINS, M. D. |
| 11:15 A. M.—12:00 Noon | Treatment of Osteoarthritis | R. L. HADEN, M. D. and W. J. ZEITER, M. D. |
| 12:00 Noon— 1:00 P. M. | Luncheon | |
| 1:00 P. M.— 2:00 P. M. | Demonstration of Dermatological Patients | GEO. H. CURTIS, M. D. |
| 2:00 P. M.— 2:45 P. M. | Differential Diagnosis of Common Dermatoses | GEO. H. CURTIS, M. D. |
| 2:45 P. M.— 3:30 P. M. | Principles of Treatment of More Common Dermatoses | E. W. NETHERTON, M. D. |
| 3:30 P. M.— 4:00 P. M. | Hyperthyroidism in Young and Old | GEORGE CRILE, Jr., M. D. |
| 4:00 P. M.— 4:45 P. M. | Treatment of Encephalitis and Its Sequelae | JOHN TUCKER, M. D. |
| 6:00 P. M. | Dinner | |
| 8:00 P. M. | Frank E. Bunts Lecture | FRANCIS BENEDICT, M. D. |

## Wednesday, November 15, 1939

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|---|---|---|
| 9:00 A. M.— 9:45 A. M. | Neurosyphilis, Neurorecurrences, Wassermann-Fastness, etc. | E. W. NETHERTON, M. D. |
| 9:45 A. M.—10:30 A. M. | Clinical Problems in Gallbladder Disease | R. S. DINSMORE, M. D. |
| 10:30 A. M.—11:15 A. M. | Ureteral Obstruction—X-ray Diagnosis | B. H. NICHOLS, M. D. |

## Wednesday, November 15, 1939—Continued

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| 11:15 A. M.—12:00 Noon | X-ray Diagnosis of Lesions of the Colon | J. C. ROOT, M. D. |
| 12:00 Noon— 1:00 P. M. | Luncheon | |
| 1:00 P. M.— 2:00 P. M. | Demonstration of Patients—End Results in Carcinoma of the Colon and Rectum | T. E. JONES, M. D. |
| 2:00 P. M. | SYMPOSIUM: The Treatment of Medical Emergencies | |
| | Cardiovascular | A. C. ERNSTENE, M. D. |
| | Diabetes, Endocrine | E. P. MCCULLAGH, M. D. |
| | Gastro-Intestinal | E. N. COLLINS, M. D. |
| | Hayfever, Asthma, Hives | J. W. THOMAS, M. D. |



## REGISTRATION BLANK

....., 1939

THE FRANK E. BUNTS INSTITUTE
Cleveland Clinic
Cleveland, Ohio
*Gentlemen:*

Please register me for the course in "Diagnosis and Treatment" which is to be given November 13, 14, and 15, 1939.

I am enclosing a check for $5.00, and the remainder of the fee, $5.00, will be paid on registration, November 13.

NOTE: Checks should be made payable to The Frank E. Bunts Institute and sent to A. D. Ruedemann, M. D., Cleveland Clinic, Cleveland, Ohio.

Name .....

Address .....

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Medical School from which Graduated

# Exhibits

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| Roentgen Findings in Ureteral Obstruction | B. H. NICHOLS, M. D. |
| Roentgen Findings in Diseases of the Colon | J. C. ROOT, M. D. |
| Endocrine Disturbances | E. P. McCULLAGH, M. D. AND E. J. RYAN, M. D. |
| Allergy Exhibit | J. W. THOMAS, M. D. AND C. R. K. JOHNSTON, M. D. |
| Bronchoscopy Exhibit | PAUL M. MOORE, M. D. |
| Intravenous Urography | W. J. ENGEL, M. D. |
| Tumors of the Esophagus and Stomach | E. N. COLLINS, M. D. AND R. J. F. RENSHAW, M. D. |

*Mail registration blank to*

DR. A. D. RUEDEMANN, Cleveland Clinic

Cleveland, Ohio.

## CONTRIBUTORS



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